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VOLUME SEVENTY-ONE

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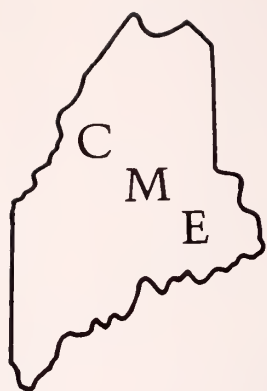
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CONTINUING MEDICAL EDUCATION IN MAINE

Hospital Activities

Augusta Mental Health Institute Augusta, Maine

- Dec. 11, 1980 **Special Issues in Family Therapy Training**
10-11:30 a.m. Leonard Siegel, M.D., Augusta Mental Health Institute
- Dec. 18, 1980 **Possible Genetic Sensitivity to**
10-11:30 a.m. **Hallucinogens—Drugs**
Henry Abraham, M.D., Harvard Medical School; Massachusetts General Hospital

These sessions are Grand Rounds. All programs have been certified AMA and LCCME Category I. For further information contact Pauline Soper; 622-3751.

Eastern Maine Medical Center Bangor, Maine

- | | | |
|------------|----------------------------------|----------------|
| 1st Mon. | EEG Conference | 12-1 p.m. |
| 1st Mon. | Weekly Surgical Service Rounds | 5-6 p.m. |
| 2nd Mon. | EEG Conference | 12-1 p.m. |
| 2nd Mon. | Weekly Surgical Service Rounds | 5-6 p.m. |
| 3rd Mon. | EEG Conference | 12-1 p.m. |
| 3rd Mon. | Weekly Surgical Service Rounds | 5-6 p.m. |
| 4th Mon. | EEG Conference | 12-1 p.m. |
| 4th Mon. | Weekly Surgical Service Rounds | 5-6 p.m. |
| 4th Mon. | ENT Section Meeting | 12-1 p.m. |
| 1st Tues. | Surgical Service Review Meeting | 12-1 p.m. |
| 2nd Tues. | Family Practice Service Meeting | 6:30-7:30 p.m. |
| 2nd Tues. | Pulmonary Medicine Section Conf. | 8-9 a.m. |
| 3rd Tues. | Dermatology-Pathology Conference | 5-6 p.m. |
| 1st Wed. | Ophthalmology Section Meeting | 7:30-8:30 p.m. |
| 1st Wed. | Tumor Clinic Conference | 2-5 p.m. |
| 1st Wed. | Radiology Conference | 5-6 p.m. |
| 2nd Wed. | Tumor Clinic Conference | 2-5 p.m. |
| 2nd Wed. | Radiology Conference | 5-6 p.m. |
| 3rd Wed. | Tumor Clinic Conference | 2-5 p.m. |
| 3rd Wed. | Radiology Conference | 5-6 p.m. |
| 4th Wed. | Tumor Clinic Conference | 2-5 p.m. |
| 4th Wed. | Radiology Conference | 5-6 p.m. |
| 1st Thurs. | Ophthalmology Section Meeting | 7:30-8:30 a.m. |
| 1st Thurs. | OB-GYN Conference | 8-9 a.m. |
| 1st Thurs. | Pediatric Grand Rounds | 9-10 a.m. |
| 1st Thurs. | Medical Service Meeting | 10-11:15 a.m. |
| 1st Thurs. | Cardiology Conference | 11 a.m.-1 p.m. |
| 2nd Thurs. | OB/GYN Conference | 8-9 a.m. |
| 2nd Thurs. | Pediatric Grand Rounds | 9-10 a.m. |
| 2nd Thurs. | Medical Service Meeting | 10-11:15 a.m. |
| 2nd Thurs. | Cardiology Conference | 11 a.m.-1 p.m. |

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| 2nd Thurs. | Surgical Service Meeting | 7:45-9 a.m. |
| 3rd Thurs. | OB/GYN Conference | 8-9 a.m. |
| 3rd Thurs. | Pediatric Grand Rounds | 9-10 a.m. |
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| 4th Thurs. | OB/GYN Conference | 8-9 a.m. |
| 4th Thurs. | Pediatric Grand Rounds | 9-10 a.m. |
| 4th Thurs. | Medical Service Meeting | 10-11:15 a.m. |
| 4th Thurs. | Orthopedic Service Meeting | 7:30-9 a.m. |
| 4th Thurs. | Urology Section Meeting | 7:30-8:30 a.m. |
| 4th Thurs. | Surgical Service Death Review | 7:45-9 a.m. |
| 1st-4th Fri. | Neurology Grand Rounds | 8-9 a.m. |

Visiting Professor Program:

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| 2nd Thurs. | Medical Service Visiting Professor | 10 a.m.-5 p.m. |
| 4th Thurs. | Pediatric Service Visiting Professor | 10 a.m.-5 p.m. |
| as scheduled | Surgery Service Visiting Professor | |
| as scheduled | Orthopedic Service Visiting Professor | |
| as scheduled | Family Practice Visiting Professor | |
| as scheduled | Psychiatric Service Visiting Professor | |
| as scheduled | OB/GYN Service Visiting Professor | |

All activities have been certified AMA and LCCME Category I. For further information contact James F. Lawsing, III, M.D.; 947-3711 Ext. 2303.

Henrietta D. Goodall Hospital Sanford, Maine

- Dec. 18, 1980 **Office Dermatology**
Douglas Wooldridge, M.D., Harvard Medical School, Boston, Massachusetts
- Jan. 20, 1981 **Blood Gases, Fluids, and Electrolytes**
Charles Lipson, M.D., Wellesley Hospital, Newton, Massachusetts; Tufts University School of Medicine, Boston, Massachusetts

These meetings will be held at the H.D. Goodall Hospital's Conference Room at 7 p.m. These programs have been certified AMA and LCCME Category I, AAFP (applied for) and Maine Pharmaceutical Association credit. For further information contact Melvin Bacon, M.D.; 324-3632.

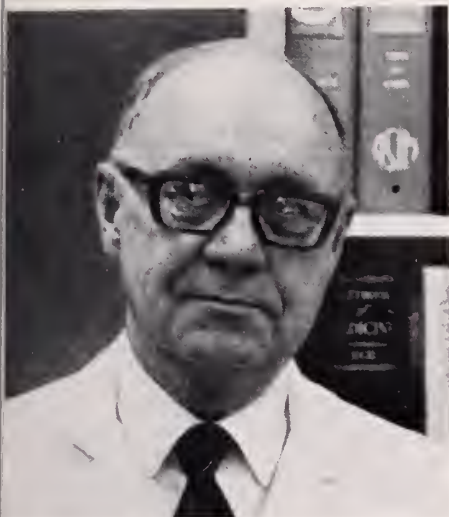
A.R. Gould Memorial Hospital Presque Isle, Maine

- Dec. 15, 1980 **Sidney Farber Cancer Institute Speaker**
This meeting is a Grand Round and begins at 7:30 p.m. in the Rotary Regional Educational Center at A.R. Gould Memorial Hospital. This program has been certified AMA and LCCME Category I. For further information contact Marilyn Dean; 769-2511.

Continued on Page 387

"THE PHYSICIAN IS A DECISION MAKER, AND ALMOST EVERY DECISION HE MAKES COSTS OR SAVES MONEY."

—Dr. William Felts, Past President,
American Society of Internal Medicine



More and more physicians today are beginning to realize the extent of the economic influence they have, and are finding ways of holding costs down.

A number of studies show that the more physicians *know* about costs, the more they try to *reduce* them.* And this reduction can be done without reducing the quality of care to the patient.

How are they doing this? As a start they have become thoroughly familiar with the costs they incur on behalf of their patients. They know how much an X-ray costs, how much their

hospital charges for routine lab tests. They're requesting copies of patients' hospital bills. And asking their hospitals to print the charges for diagnostic tests right on the order sheet.

What else are physicians doing? Minimizing their patients' hospital stays, whenever possible. Reevaluating routine admissions procedures. Questioning the real need of the diagnostic tests they order for their patients. Avoiding duplicate testing. Trying to discourage their patients' demands for unnecessary medication, treatment or hospitalization. Compiling daily logs of their medical decisions and what they cost. And more.

More physicians today realize what a tough problem we're all faced with. They know this is a challenge for medicine. And that physicians are in the best position to deal with and solve the problem.

*PATIENT CARE Magazine—Outlook 1977 "Face-Off: Cost Containment vs. Chaos," January 1, 1977

Lyle CB, et al. "Practice habits in a group of eight internists," ANNALS OF INTERNAL MEDICINE 84 (May 1976), 594-601.

Schroeder SA, et al. "Use of laboratory tests and pharmaceuticals: variation among physicians and effect of cost audit on subsequent use," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 225 (Aug. 20, 1973), 969-73.



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The Journal of the Maine Medical Association

Volume Seventy-one

Augusta, Maine, January 1980

Number 1

Thrombocytopenia as a Leukemic Prodrome

EUGENE M. BEAUPRE, M.D.*

Despite several new diagnostic laboratory tests¹⁻⁵ which help predict which of a number of hematologic disorders will eventuate as leukemia, "preleukemia" can be diagnosed with absolute certainty only when the patient has ultimately developed typical leukemia, usually acute non-lymphocytic, and then retrospectively. The term, preleukemia, was coined by Block in 1953⁶. Initially it was felt to be an uncommon entity, but in more recent series of acute, non-lymphocytic leukemia, 30-60 percent of patients have had a preleukemic phase to their disease.⁷

Linman⁸ has attempted, using retrospective analysis of 34 cases, to define the entity preleukemia. Seventy percent of cases of preleukemia occurred in patients fifty years of age or older; median age was about sixty years. Early symptoms were absent or non-specific in about half the patients. Most of the remaining cases had symptoms secondary to anemia. Physical findings were likewise non-specific; splenomegaly was rare.

Linman⁸ finds hematologic abnormalities "quite uniform and constant." Anemia, neutropenia, and thrombocytopenia occur alone or in varying combinations. Anemia is almost always present and associated with varying sized and shaped red cells, prominent oval macrocytosis, normochromic red cells (but occasionally with a two red cell population with varying numbers of hypochromic red cells). Circulating nucleated red cells are present in about two-thirds of cases.

Most patients have neutropenia. With careful search, an occasional immature granulocyte or monocyte can be found in stained blood smears. Auer bodies are uniformly absent.

Thrombocytopenia occurs in most patients, but it is seldom the dominant finding. In the Mayo Clinic series,⁹ only one of 34 patients had predominant thrombocytopenia. Bone marrows frequently show

iron overload with "ringed sideroblasts." Red cell precursors are frequently megaloblastoid.

We have recently seen two patients at the Mid-Maine Medical Center with seemingly isolated thrombocytopenia who ultimately developed acute leukemia. Both were male children whose clinical and hematologic findings initially in no way suggested abnormalities of other marrow cell lines except for the expected iron deficiency anemia which commonly complicates thrombocytopenic purpura because of chronic blood loss.

CASE REPORTS

J.M., a six-year-old male, was found to be thrombocytopenic when he developed purpura in April 1977. Initially his platelet count was 55,000, and his symptoms mild. It was felt that this was probably a post-viral thrombocytopenia, so he was watched carefully on an outpatient basis. Finally his platelet count fell to 30,000 per cubic millimeter, so he was hospitalized at the Mid-Maine Medical Center May 1, 1977. The only therapy he had received prior to the onset of his thrombocytopenia was Kwell for presumed scabies. He had had clinically bothersome purpura on only one occasion following a bout of protracted crying and coughing.

By physical examination, he was afebrile and appeared well developed and well nourished. There was no clinical purpura at the time of admission. Hemoglobin was 10.9 gm.% and hematocrit 32%. Indices were hypochromic and microcytic. Leukocyte counts were 5,200 and 5,400 per cubic millimeter with 58% neutrophils, 1% stab cells, 31% lymphocytes, 8% monocytes, and 2% eosinophils. Platelet counts were 38,000 and 44,000 per cubic millimeter. Bone marrow was hypercellular with normal myeloid to erythroid ratio. There was no stainable iron in the bone marrow. The outstanding abnormality in the bone marrow was a markedly reduced number of megakaryocytes. Prothrombin time was 13.4 seconds (control 12.3 seconds). Partial thromboplastin time was 27.9 seconds (control 27.9 seconds). Chest x-ray and uric acid levels were normal. Serum iron was 61 micrograms percent, and iron binding capacity 260 micrograms percent. Folic acid was 11 nanograms per deciliter and B-12 markedly elevated at 3,050 picograms per deciliter.

Tentative diagnosis of idiopathic thrombocytopenic purpura was made, but the reduced number of megakaryocytes was felt to be atypical. He was treated with corticosteroids, oral iron, and oral folic acid.

On August 17th, his hemoglobin was 11.8 gm.% and hematocrit 34%. Leukocyte count was 9,000 per cubic millimeter, with a nor-

*Mid-Maine Medical Center, Waterville, Maine 04901.

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mal differential count. Platelets were still reduced at 64,000 per cubic millimeter. Red cell indices were still hypochromic and microcytic. He had an active summer with very little bruising. Appetite was good, and weight gain and development were normal.

In late September, he developed increasingly severe bruising; his platelet counts fell despite continued treatment with corticosteroids. He was readmitted November 13, 1977, for further study.

Physical examination was unchanged except for purpura. Liver and spleen were normal in size, and there was no clinically apparent lymphadenopathy. At the time of admission his hemoglobin was 9.7 gm.% and hematocrit 28.5%. Corrected leukocyte count was 10,400 per cubic millimeter. Differential count showed 34% polymorphonuclear leukocytes, 50% lymphocytes, 9% monocytes, and 1% myelocytes. There were 6 nucleated red cells per 100 white cells on the smear. Platelet count was 20,000 per cubic millimeter. The serum B-12 levels were again elevated at over 2,000 picograms per deciliter. Folic acid level was 20 nanograms per deciliter. Bone marrow aspirate at this time was very different. Red cell morphology was now clearly megaloblastoid, but there were no Auer rods seen. Ten percent of the white cells series were blast forms. Again there were very rare megakaryocytes, and there was no stainable iron. Consultation was sought from Frank Oski, M.D., pediatric hematologist and Chief of Pediatrics at Upstate Medical Center in Syracuse, New York. He felt that the patient had "smoldering acute non-lymphocytic leukemia." He did not feel that we should initiate treatment at this time, but should wait until the disease was more blatantly active.

The patient was readmitted to the hospital November 27, 1977, with a fever of 104.4 degrees. By physical examination he was pale, but still well developed and in no acute distress. There was generalized lymphadenopathy with enlargement of the spleen to 2½ cm. below the left costal margin. Liver was enlarged 1 cm. below the right costal margin. Hemoglobin was 6.3 gm.% and hematocrit 19%. Indices were now normal. Leukocyte count was 5,600 per cubic millimeter with 30% polymorphonuclear leukocytes, 39% lymphocytes, 20% monocytes, 2% eosinophils, 1% metamyelocytes, 1% myelocytes, 5% progranulocytes, and 2% blast cells. There were 3 nucleated red blood cells per 100 white blood cells. Platelet count was 10,000 per cubic millimeter. Appropriate cross match was difficult because of the presence of an anti I antibody in a concentration of 1:256. All cultures, blood, urine, and throat, were sterile. Chest x-ray and sinus x-rays were normal. The infectious disease consultant felt that this was a non-bacterial illness. He was transfused to a level of 11.7 gm.%, and within four days was afebrile and well without antibiotics.

He was readmitted December 15, 1977, with severe epistaxis. Blood pressure was only 60/40, and he was clinically very pale. Liver was enlarged 4 cm. below the right costal margin, and spleen 4 cm. below the left costal margin. Hemoglobin was 4.7 gm.%, and hematocrit 14%. Leukocyte count was 13,700 per cubic millimeter with a differential count very much like the one during his November admission. He was given 2 units of packed red cells and 6 units of platelets; this resulted in a hemoglobin of 11.4 gm.%. He was transferred to the Boston Children's Hospital where he was treated with Vincristine-Adriamycin-Cytosine arabinoside. He achieved a partial remission, but thrombocytopenia persisted despite platelet transfusions from his parents. No antibody was found to platelets *in vitro*, but the presence of platelet antibodies was strongly suspected on clinical grounds. Finally a "desperation splenectomy" was done, but the platelet level could still not be attained at over 10,000 per cubic millimeter. He developed postoperatively anasarca and azotemia. He was dialyzed on two occasions, but died February 6, 1978. Final diagnosis was acute non-lymphocytic leukemia.

S.S., a Caucasian male born November 8, 1970, was admitted to the Yale-New Haven Hospital in February 1972, referred by his family doctor because of bruising and oral bleeding secondary to tooth eruptions. At that time his platelet count was found to be 42,000 per cubic millimeter, and reticulocyte count 5.2%. Bone marrow was normal with adequate megakaryocytes. A tentative diagnosis of idiopathic thrombocytopenic purpura was made, and therapy withheld because of the mildness of the symptoms. In the summer of 1972 he was admitted to a Boston hospital, while on

vacation, for epistaxis. He was treated with platelet concentrates and corticosteroids. The bleeding stopped promptly, but the response to steroids was suboptimal with a peak count of about 125,000 per cubic millimeter. He was readmitted to the Yale-New Haven Hospital in November 1972, to rule out familial thrombocytopenias such as the one associated with the Wiskott-Aldrich syndrome. Survival time of mother's platelets in the patient was normal, whereas survival time of pooled heterologous platelets was markedly reduced. Coombs' tests were negative, and the antinuclear antibody levels were normal. Isohemagglutinins, quantitative immunoglobulins, and blast transformation of lymphocytes in the presence of phytohemagglutinin were all within normal limits. Delayed hypersensitivity to the candida and trichophyton antigens were intact. Persistent fetal hemoglobin made up 10 percent of the total hemoglobin by electrophoresis. Hemoglobin level was 13.1 gm.%, leukocyte count, 11,100, with a normal differential count, and platelet counts varied between 30,000 and 75,000. The nature of the thrombopenia was obscure, especially in the face of normal maternal platelet survival.

He was readmitted to the Yale-New Haven Hospital in coma on December 5, 1972. He had had a runny nose for eight days and fever for four days. Two days before admission he had received 2 teaspoons of Polycillin® from his family doctor. On the evening of admission, he was found lying with his head deviated to the right and his eyes rolled upward and to the right. By physical examination, he had a central right facial weakness and right hemiparesis, worse in the arm than the leg. Lumbar puncture showed 1,368 red cells per cubic millimeter, 120 leukocytes per cubic millimeter, with a differential of 93% polys, protein level of 95 mg.%, and sugar of 90 mg.%. Peripheral leukocyte count was 12,360 per cubic millimeter, and platelet count 24,000 per cubic millimeter. Cultures of cerebrospinal fluid, blood, urine, and pharynx grew out no pathogens. Viral cultures of the rectum, throat, and cerebrospinal fluid were sterile.

He was given 5 units of platelets on admission; this resulted in a rise of platelet count from 24,000 to 39,000 per cubic millimeter. He was also treated with Ampicillin, 300 mg. per kilogram intravenously. He improved slowly, but was left with considerable weakness of the right arm and leg. The final diagnosis was felt to be viral meningoencephalitis.

At this time his family moved to Maine. Within three or four months his neurologic symptoms and signs had cleared completely. He developed adenoidal enlargement with repeated bouts of otitis media and some conductive hearing loss. So that he could be evaluated for adenoid surgery, he was readmitted to the Yale-New Haven Hospital for a one day stay October 26, 1973. At that point his weight was 14.65 kilograms (50-75th percentile), and his height 101 cm. (90th percentile). By physical examination, he had rare ecchymoses over the anterior tibial surfaces. He had bilateral serous otitis media. Liver and spleen were not enlarged. He was now neurologically normal.

On this admission, his hemoglobin was 12.2 gm.% and his platelet count 18,000 per cubic millimeter. Leukocyte count was 7,200 with a normal differential. Prothrombin time and partial thromboplastin time were within normal limits. Immunoglobulins, complement levels, sugar, and BUN were all normal. Antibody response to bacterial antigens were all normal. Bilateral conductive hearing loss was confirmed by audiogram. It was recommended that a trial of decongestants be given. If these did not improve the serous otitis media, it was suggested that he be given Prednisone in preparation for surgery. Prednisone was tried, but platelets did not respond adequately. Finally on February 4, 1974, he was admitted with a temperature of 103 degrees and an acute left middle ear infection. Hemoglobin was 11.6 gm.% and hematocrit 35%. Leukocyte count was 14,600 per cubic millimeter with 74% polys, 6% stab forms, 13% lymphocytes, and 7% monocytes. Platelet count was 48,000 per cubic millimeter. Bilateral poly tube insertions were complicated by bleeding. Ten units of platelet-rich plasma were given on the first postoperative day. Although the platelet count rose to only 59,000, the bleeding stopped promptly. He was given oral Ampicillin throughout the hospitalization. Within four days of surgery, there was complete resolution of his fever.

He did very well until December 1974, when he developed fever and watery diarrhea. He was admitted December 24, 1974, with large numbers of petechiae, moderate numbers of ecchymoses,

and a mild erosive stomatitis. Liver and spleen were not enlarged and there were no palpable lymph nodes.

On admission his hemoglobin was 3.5 gm.% and his hematocrit 11%. Leukocyte count now was 1,800 with 100% of what were initially felt to be atypical lymphocytes by differential count. Reticulocyte count was 0% and platelet count 16,000 per cubic millimeter. He was promptly transfused with 2 units of packed red cells. Blood cultures grew staphylococcus aureus for which he was started on Staphicillin® and Garamycin®. Bone marrow revealed complete replacement of the marrow by lymphoblasts. It should be pointed out that this was almost three years after the thrombocytopenia was first documented, and over three years after the onset of his bleeding symptoms. Remission was induced using Vincristine and Prednisone. Complete remission, documented by bone marrow aspiration, was achieved easily, and he was given prophylactic cranial radiation and intrathecal Methotrexate starting in February 1975. Maintenance therapy was made up of Prednisone, Methotrexate, and 6 Mercaptopurine as outlined in protocol 1173 supervised by O. Ross McIntyre, M.D. of Dartmouth Medical School. Bone marrow was normal June 12, 1975, but thrombocytopenia of 25,000 per cubic millimeter persisted. By September 25, 1975, the platelet count was 100,000 per cubic millimeter. Hemoglobin level was 12.5 gm.%, leukocyte count 3,300 per cubic millimeter, and differential count normal.

On October 7, 1975, he was admitted as an emergency with weakness of the right face and flaccid weakness of the right arm and leg. Hemoglobin was 10.6 gm.% and hematocrit 31%. Leukocyte count was 3,000 per cubic millimeter and the differential count was normal. Platelet count was 98,000 per cubic millimeter. Bone marrow examination continued to show remission, but lumbar puncture revealed occasional mitotic lymphocytes in the cerebrospinal fluid. His condition deteriorated rapidly, and he died at 5:30 A.M. on October 16, 1975. Autopsy showed organ and bone marrow remission, but histologically the brain showed mild lymphoblastic infiltration with extensive hemorrhage.

Although both these children were treated as though they had idiopathic thrombocytopenic purpura, each had findings atypical for that entity. In the first case, megakaryocytes were reduced in number whereas in idiopathic thrombocytopenic purpura megakaryocytes are present in normal or increased numbers. In the second case, survival of maternal platelets were normal, although pooled platelets had a markedly shortened platelet survival time. Both patients responded suboptimally to corticosteroids.

Congenital thrombocytopenias, i.e., Fanconi syndrome, Wiskott-Aldrich syndrome, and the May-

Hegglin anomaly, were ruled out on both clinical and laboratory grounds. Both were in the age group, two to eight years, in which childhood idiopathic thrombocytopenic purpura is most common.¹⁰ Therefore, a tentative diagnosis of atypical idiopathic thrombocytopenic purpura was made in each instance.

The second case is unusual in that it is one of the very rare instances in which a preleukemic phase has been documented in acute lymphocytic leukemia.^{11,12}

As hematologic laboratory evaluations become more routine, one increasingly finds earlier, less-diagnostic features of hematologic illnesses. One preleukemic entity has been well described by Linman. It seems likely that more hematologic syndromes will be described that are "preleukemic." From our experience, we would like to suggest that in rare cases isolated atypical thrombocytopenias may be still another preleukemic syndrome.

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Spring Meeting of the M.M.A. House of Delegates

Saturday, March 22, 1980

Mid-Maine Medical Center (Thayer Unit), Waterville, Maine

12:30 P.M.—Registration; 1:00 P.M.—Lunch; 2:00 P.M.—Meeting

9:30 A.M.—Meeting of the Executive Committee

Status of Emergency Medical Care in a Rural State

Experience in Maine, 1975-1979

H. ALAN HUME, M.D., F.A.C.S.*

Passage of the Emergency Medical Services Systems (EMSS) Act has helped provide a mechanism and funding base to develop and improve regionalized basic (BLS) and advanced life support (ALS) systems throughout the State of Maine. These developments have had as their central theme a broad-based multi-disciplinary educational effort. The principle emphasis to date has been upon emergency cardiac care. Pre-hospital ALS systems at the advanced EMT-cardiac level are currently operational in the greater Portland, Lewiston/Auburn, greater Waterville and Skowhegan areas. Impact of these systems on patient outcome will be the subject of a subsequent report. Synchronous with these developments has been the delivery of Advanced Cardiac Life Support training programs to more than two thousand physicians and nurses throughout the state. The probability of survival from out-of-hospital/emergency department cardiac arrest still varies throughout the state but has clearly improved during the past four years.

Nationally, and in Maine, there has been a marked improvement in the pre-hospital phase of emergency medical care. However, documentation of the continued failure of the hospital phase of emergency care for severely traumatized patients continues to accumulate. Reports from Vermont,¹ Maryland,² Utah,³ New York,⁴ Wisconsin,⁵ and California,⁶ support the allegation⁷ that hospital care of the critical trauma patient has not improved significantly since VonWagoner's initial report⁸ in 1961.

The following case reports suggest that the situation is no different in Maine but also show that appropriate initial treatment and stabilization with referral to a regional center prepared to receive and treat severe trauma patients can result in survival despite potentially lethal injuries.

CASE REPORTS

Case 1

This young patient struck a tree while driving a motorcycle. The patient was transported to a local hospital and seen by a physician approximately one hour post-injury. The patient was unconscious and was intubated because of "obstructed respirations." Multiple extremity fractures were diagnosed clinically. No vital signs were recorded during a 15 minute stay in the emergency room. An i.v. of 5% D/W was started and the patient was transferred to another hospital unaccompanied by personnel trained in ventilatory support. The patient suffered a cardiac arrest 40 minutes prior to arrival at the receiving hospital where she was pronounced dead on arrival.

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Case 2

This middle-aged patient was involved in an automobile accident as the result of an intersection collision. Diagnoses at the scene by pre-hospital personnel included flail chest, head injury, possible fracture of both lower extremities, possible fractured pelvis, fractured wrist, and possible internal bleeding. Extrication required 20 minutes and the patient was seen in an emergency department 35 minutes after the accident.

Emergency Department diagnoses included left flail chest, multiple maxillofacial fractures, obstructed airway, bilateral hip and wrist fractures. Blood pressure on arrival was 150/100 but pulse rate and respiratory rate were not recorded. Multiple i.v. lines were established and the patient received 2500 cc. of lactated-Ringers solution during the next 60 minutes.

Clinical examination revealed an unconscious patient with decreased breath sounds bilaterally, extensive maxillofacial injuries and a flail chest. The patient was intubated 40 minutes after arrival at an emergency department. Arterial blood gas determinations were not done.

X-rays revealed multiple rib fractures on the left with a moderate amount of subcutaneous air. Extensively comminuted central fracture-dislocations of both hips with marked posterior displacement were noted.

The patient expired in the emergency department approximately one hour after arrival at the hospital.

Case 3

This young female was thrown from her bicycle striking her head, which rendered her immediately unconscious. She was transported to a local hospital by ambulance where generalized convulsions, a dilated left pupil, and a persistent unconscious state were noted. Ventilatory assistance was provided by a nurse who accompanied the patient during secondary transfer. The local attending physician called the emergency department at the nearest regional center to coordinate the patient's care.

The patient received pharmacologic doses of dexamethasone on arrival at the referral hospital. Vital signs remained normal and a CAT scan was done 30 minutes after arrival. Lateral cervical spine x-rays in the emergency department were normal and a fracture of the right temporal bone was noted. There was evidence of papilledema with venous congestion and retinal hemorrhages.

The patient was operated immediately after completion of the CAT scan which showed a left subdural hematoma and a right temporal intracerebral hematoma. A Richmond screw was inserted and intracranial pressure monitored for 72 hours. After recovery of consciousness, the patient manifested mental confusion and garbled speech for several days. The patient was discharged on the 14th post-injury day with normal speech and mental alertness and without demonstrable neurologic deficit.

DISCUSSION

In defining quality of care problems, it becomes evident that patients with moderate to severe injuries are still faced with unacceptable mortality and morbidity rates. Exactly how low a mortality rate can be achieved in a state with large rural areas and widely dispersed medical facilities remains a major health policy question.

Abdominal and extremity injuries not associated with central nervous system or respiratory system injuries are generally adequately managed. The man-

agement of head and chest injuries requires considerably more emphasis in continuing education programs for physicians. Most patient management problems are due to failure to act rather than inappropriate diagnosis and action. Emphasis on the practical and technical aspects of trauma care will be included in Advanced Trauma Life Support (ATLS) courses to be delivered Statewide beginning in early 1980.

Definition of the magnitude of the trauma problem and a methodology to evaluate quality of care⁹ is needed in order to design an appropriate system of trauma care for the State of Maine.

Boyd¹⁰ has suggested that the establishment of several model demonstration trauma centers of excellence might be of value in the development of a standardized data base to help overcome many of the limitations of our knowledge of the trauma problem.

Guidelines published by the Committee on Trauma of the American College of Surgeons¹¹ represent current thinking on structural and process measures which may effect patient outcome.

In an effort to ameliorate the existing pandemic of trauma, currently estimated to represent a \$60 billion cost nationally, the Department of Human Services, Maine physicians, nurses, hospital administrators and EMS project staff have developed a collaborative trauma research project with the University of Wisconsin Center for Health Systems Research and Analysis to address these issues.¹² This three year research study will begin in early 1980 in an attempt to answer the following questions:

1. Does where (what hospital) a patient is treated make a difference in patient outcome?
2. How much does a categorization system influence where the patient is treated?
3. What categorization criteria are most associated with outcome?
4. What characteristics of the between hospital transfer process are most associated with patient outcome?
5. What seem to be the underlying problems causing differences in outcome between hospitals treating patients with similar severity indices?

6. What emergency department, in-hospital and pre-hospital factors are most closely associated with outcome differences?
7. What are the costs and benefits of alternative solutions to problems causing these outcome differences?

CONCLUSION

Improvements in care of the trauma patient in Maine have lagged behind improvements in care for patients with acute cardiac emergencies. The broader spectrum of physiologic derangements seen in multiple injury patients is a significant factor in this difference.

A three year research project to establish a reliable data base to include severity indices, morbidity indices, and quality of care indices has been initiated. Advanced Trauma Life Support (ATLS) training programs will be initiated in early 1980 on a Statewide basis.

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Adult Onset Stuttering

A Case Report

H. WAYNE TOBIN, M.D.* AND BRUCE D. OLSEN, PH.D.**

Stuttering is a complex phenomenon which is found primarily in childhood. Its onset in adulthood is rare.

The following case is presented for several reasons: (1) It originates in a woman of late middle age, (2) Speech examination shows numerous characteristics atypical of stuttering behavior.

CASE PRESENTATION

E.S. is a 58-year-old married, white female who requested psychiatric evaluation because of the onset of stuttering. Approximately one year prior to evaluation, the stuttering commenced several hours after an automobile accident in which she was involved. The stuttering has been continuous since the day of the accident. According to the patient, she "blackened out for several minutes," but was not hospitalized. However, she describes her feelings after that day as jittery and anxious and noticed the onset of stuttering. She denies feeling depressed or sad before or after the accident, likewise denies any problem at work or home prior to or since the accident. She has been seen by a neurologist and is neurologically clear. Her only medication has been occasional Meproamate without any effect. Other than the stuttering, she has noticed only generalized feelings of anxiety when riding as a passenger in a car. The only other complaints have been occasional neck pain when turning her head. Sleep, appetite, weight and sexual activity are unchanged. Interest and performance in activities such as work are unaffected. No history of neurotic or psychotic symptomatology.

Past History

Negative for history of prior psychopathology, either occupational, marital or genetic-familial. There is no history of major prior trauma.

Mental Status Examination

She is a tall, well developed, well nourished woman oriented times 3. Cognitive function intact. No gross disorder of thought form, content or stream. Mood was euthymic. Anxiety appeared in the form of diaphoresis and frequent shifting in her seat when pressured to do serial 7's. Concentration was diminished under pressure during the interview. She was generally affectively constricted but not inappropriate.

Results of Speech and Audiological Examination

According to one of the authors (B.O.), this woman's stuttering violates some basic rules and behaviors. Typically, her stuttering appeared to be repetitious of initial sound with prolongation of some sounds, and occasional larynx tension on vowels. All blocks were not on the initial syllables. Propositional speech was not more difficult than nonpropositional. In hierarchy difficulty, the patient failed to demonstrate increasing stuttering with the increase in task demand. Singing continued to produce speech block, and rhythm repetition did not correct the disfluency. She also failed to adapt to repetitive reading, i.e., the number of blocks in her speech did not decrease. Instructed voice pitch change did not affect the stuttering. Her hearing test was essentially non-revealing. Whispering produced no change. These characteristics, i.e., failure of adaptation, non-modifiability with singing, whispering or pitch change, non-alteration with propositional speech vs.

nonpropositional speech and failure to respond to hierarchy, are all atypical and highly unusual for classical stuttering.

DISCUSSION

Stuttering as a speech disorder is currently under close scrutiny. Recent evidence indicates that it is not a unitary disorder and indeed can occur under different psychological and physical settings. A general definition of stuttering would include: an interruption in the free fluency or flow of speech so as to interfere with verbal communication. One exclusion criterion would be the presence of mechanical cause in the vocal mechanism.

Characteristics of typical stuttering include a tendency for repetition of syllables and word sounds, often initial word sounds. Other defining phenomena include prolongation or "drawing out" of sounds especially vowels, and sound blocks or silences. Limbic, facial or trunk movements associated with the escape from the sound block phenomena are frequent. Additionally, avoidance behavior of situations which provoke stuttering, are evident.

Epidemiologically, stuttering occurs in 1% of school age children in the United States and England. As mentioned, its onset in adult life is rare. Sex ratios vary from 3:1 to 10:1 depending on the study, with males predominating. There appear to be no socioeconomic patterns. Its occurrence de novo in adulthood (according to Beech) is associated almost exclusively with sudden and intense physical or psychological stress.

Theoretical formulations reflect the lack of unifying concepts. Stuttering has been seen as a perceptual distortion in monitoring one's own speech with putative deficiency in the auditory feedback loop. Organic theorists have postulated epileptic-like and tic theories. They cite the mixed dominance and out of phase alpha waves on the EEG as supporting evidence. Other theories formulated include anxiety expectancy theory and a diagnosogenic theory of parental defining, and supportive reinforcing of stuttering phenomena in their children. Another theory depicts the anxiety reducing effects of disfluency as overruling the fear of speaking, and therefore etiological.

Snyder and others formulated many psychodynamic theories. Convincing proof for any one theory is lacking.

Research and personality theory has failed to demonstrate a pathological personality type. Role perception studies such as Sheehan's have failed to differentiate stutterers from normals. Research involving hostility or reactivity to stress phenomena,

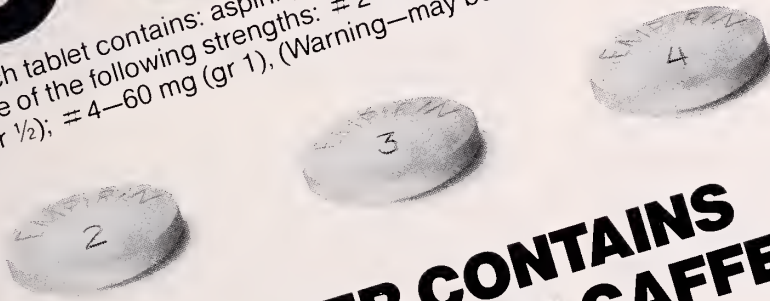
Continued on Page 11

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A Psychologist Looks at and Treats Pain

WILLARD E. MILLIS, JR., PH.D.

The involvement of psychologists in the management of patients who are experiencing pain is a relatively new development in the field of medicine. Traditionally, psychologists have been perceived as those professionals who administered psychological tests in an attempt to measure intelligence or to uncover someone's unconscious. More recently, the unique background of psychologists in personality characteristics and in behavioral techniques has been seen as a unique and complementary role in the treatment of patients who are experiencing chronic pain.

The point has been well made by many (e.g., Diggs, 1979; Fordyce, 1976) that pain is not simply a result of physical damage to tissues in the body. Expectation, suggestion, anxiety, competing psychological and sensory stimuli, and the redirection of attention have all been seen to influence the perception of pain by a patient (Degood, 1979).

A simplified way of looking at pain from a behavioral perspective can be represented by the following format:

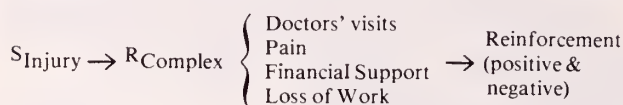


Fig. 1 A behavioral perspective of pain

A physician typically would see the pain as being caused by the injury or the stimulus, and subsequent action by the physician is usually dictated by this interpretation. Thus, the physician would take direct action to treat the injury and thus allow the tissue damage to heal and the pain to eventually diminish. Clearly, the major focus in this medical approach is upon the site of injury and upon the direct medical intervention which is dictated by that injury. A psychologist oftentimes works from the other direction, that is from the right to the left. The pain which the patient describes and complains about is seen as being a result of the positive reinforcement for the pain rather than being caused directly by the original injury. It is important to keep in mind that this interpretation is most clearly seen in the case of chronic pain where medical evaluation can not determine that any injury exists which would be compatible with the extent of pain described. These behaviors, the R_{Complex} in Fig. 1, are followed by both positive consequences and negative consequences. For example, the pain which takes place following an injury clearly is a negative consequence when first examined. However, if this pain is sufficient enough to gather sympathy from a typically abrupt and aloof spouse, then the pain also has some positive attributes as well. The balance between these positive consequences and negative consequences determines

whether or not the response complex is likely to continue.

It is just this perspective which clearly distinguishes the perspective of the psychologist from that of the physician. The medical viewpoint would see the pain, tissue damage, etc. as being a result of the injury. However, the psychologist would see much of this R_{Complex} as being controlled by its consequences. If the consequences are in the balance positive, then it is more likely that this whole complex will continue to occur. Should the consequences be in the balance negative, then it is likely that this complex would quickly become extinguished, or cease to occur. In the case of chronic pain, positive reinforcement strengthens the response complex which consists of such things as repeated doctors' visits, pain, financial support, and loss of work among other things.

When a patient is referred to a psychologist for evaluation and further treatment, there are several alternatives which must be ruled out before the diagnosis of operant pain can be made. The first is that of a basically normal personality. It oftentimes happens that patients simply have no abnormal psychological processes in operation and that the pain which they are experiencing can be explained by the physical injury which they have received. Occasionally patients are referred because no adequate basis for their pain can be found during the medical evaluation. However, it is simply not enough that they are experiencing adequate pain and no physical cause can be found for this pain. When they are found to have a basically normal personality with no suggestion of operant pain being utilized, they are referred back to the physician with a clear statement that psychological aspects are not likely to be intimately involved in the pain which they describe even though the cause is still not apparent.

The second major area which needs to be ruled out is that of malingering and simple overconcern with compensation. This is relatively infrequently encountered in practice but there are several behaviors which strongly suggest that this is the most likely explanation for the complaint. When a patient states that he must call his lawyer before taking a personality test or even before talking to the psychologist, it is usually a fair assumption that the patient is more concerned with his status regarding compensation than in finding a solution for the discomfort which he describes.

The next diagnosis which must be ruled out is that of conversion reaction, or pain which is sometimes described as being psychogenic in origin. The assumption here is that psychological problems and conflicts are unable to be appropriately expressed and are converted into physical symptoms for expression. Among the signs which strongly indicate that

conversion hysteria is the most appropriate diagnosis are the following: a uniquely characteristic profile on the MMPI, relative indifference to the discomfort and implications of the disability (la belle indifference), and finally a clear indication of strong secondary gain from the symptoms.

Only after these alternatives of normal personality, malingering, and conversion reaction are ruled out can the diagnosis of operant pain be considered. An additional complicating factor is the fact that a normal profile on the MMPI can certainly occur even when the pain is seen to be operant in nature. However, if the patient is at that point seen to be manifesting those characteristics which are typical for the operant pain syndrome, then the treatment program is begun. This treatment approach has four components.

Convincing the patient that "the pain is real" and that he is not crazy is usually the first step. Consultation with a psychologist initially causes a great deal of apprehension in the patient and this must be dealt with immediately. It is often helpful to explain the many roles that a psychologist has with emphasis upon the fact that a psychologist is something of an expert in the area of pain behavior as opposed to the physical injury which initially caused the pain. Also, it is frequently helpful to present many concrete examples of how one's psychological state determines the perception of pain. One of the easiest examples to present is the differing degree of pain which might be experienced from a broken leg if the last game of the world series is on vs. the same injury at 3 o'clock in the morning when the patient is unable to sleep.

A second vital component of treating a patient with operant pain is involvement of the immediate family members and the primary care physician. Obviously treatment will be short-circuited if the family continues to express fears that the pain is all in the patient's head and the physician continues to order more sophisticated and esoteric tests in order to track down the illusive cause of the pain. A unified front

needs to be presented to the patient which is neither judgemental or accusatory.

The third step is interviewing the patient and learning the reinforcers which continue the pain response complex. Then an attempt is made to diminish their impact. For example, if complaints of pain seem to be followed by solicitous inquiries by family or by sympathy from a formally abrupt spouse, then limiting visiting hours and the number of visitors would do much to minimize this reinforcer. Unfortunately, the characteristics of the real world oftentimes make it extremely difficult to minimize the reinforcers when they take the form of large amounts of compensation for suffering behavior and only unpleasant low-paying work for the healthy behavior.

The final aspect of treatment is to provide reinforcement for new behaviors which are incompatible with the response complex which includes pain. For example, encouraging patients to form new social contacts and experiences oftentimes allows them to gain the social stimulation which they were formally only able to obtain when they were sick and in pain. An additional way to introduce new behaviors which are incompatible with the previously learned response complex is through training the patient to control the pain experienced by self-hypnosis or the various self-regulated relaxation techniques. In addition to the proven effectiveness of these techniques in dealing with operant pain, they also have the additional benefit of being low-cost, non-habit forming, and immediately available to the patient.

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ADULT ONSET STUTTERING: A CASE REPORT—Continued from Page 8

have failed to validate any "Billy-Budd" reactions as generally applicable to stutterer responses.

Treatment approaches have been as varied as the theories. Phenothiazines, ECT, psychoanalysis, desensitization and benzodiazepines have all been tried. Based on the use of Haloperidol in Gilles de la Tourette syndrome, Murray in one study and Rosenberger in another used this medication with some benefit.

A promising technique, involves the use of delayed auditory feedback. (D.A.F.), i.e., the play back of a person's own verbal output with delays of 1/15 - 1/10 of a second. By manipulating D.A.F., one can produce stuttering in normals and reduce disfluency in some stutterers. Other techniques include speech rhythm training, rate and control training, and

shadowing. Others have attempted to use instrumental conditioning as a means of modifying stuttering. This involves desensitization and reciprocal inhibition techniques.

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CLIFFORD V. NELSON, BRIAN C. HODGKIN AND ARTHUR F. WILKINSON*

A picture of the complete M_X board is shown in Figure 1. The RCA integrated circuit is considerably less expensive than the 3629 originally used. This circuit should be used for amplifiers 1 and 2 on the M_X board, amplifier 4 on the M_Y board and amplifiers 6 and 7 on the M_Z board. No other changes are necessary.

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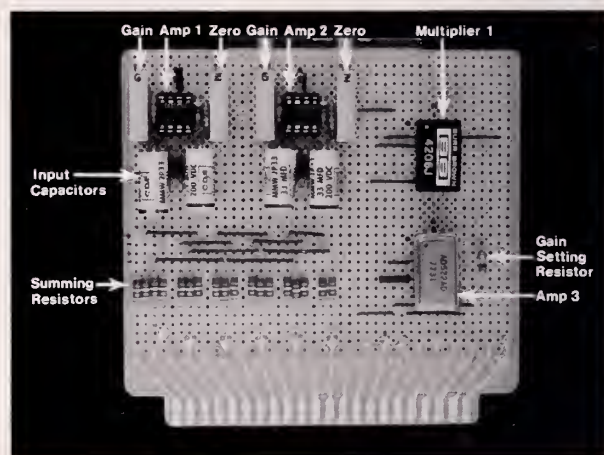


Fig. 1

Erythrocyte Deformability: The Determination of its Importance and the Importance of its Determination

JAMES M. NORTON, PH.D.*

Erythrocyte deformability is being increasingly appreciated as an important physiological concept and as a valuable indicator of clinical disorder. The ability of a red cell to traverse narrow slits or small pores determines both the time for release of young erythrocytes from the bone marrow into the peripheral circulation and the time for removal of old red cells from the blood by the spleen. Severe alterations in erythrocyte deformability may result in an inability to produce and maintain adequate circulating levels of viable, functioning erythrocytes; minor alterations may reveal subtle changes in red cell metabolic or membrane properties suggestive of, or associated with, inherited or acquired systemic disease.

The determinants of erythrocyte deformability are: (1) the elastic, viscous and bending properties of the erythrocyte membrane, the result of molecular composition, arrangement and interactions within the membrane itself; (2) the viscosity of the interior of the cell, a function primarily of the concentration and properties of hemoglobin; and (3) cell geometry, especially the relationship between surface area and volume.

Experimental methods for measuring erythrocyte deformability range from the simple to the complex in both concept and execution. The concept of membrane elasticity, for example, is relatively easy to imagine, but its determination involves precision measurements obtained by a skilled investigator using a complicated apparatus. These measurements are then subjected to a mathematical analysis using a theoretical framework that is itself often open to discussion. On the other hand, the interpretation of a simply performed measurement such as the passage time of an erythrocyte suspension through a piece of filter paper can involve a complicated consideration of many different factors and how they may interrelate with one another to produce the observed results.

Research into methods for measuring erythrocyte deformability is currently proceeding on two fronts. Simple, meaningful techniques that can be routinely performed in a clinical laboratory are being sought to

serve as a screening tool for identifying those red cell abnormalities associated with clinical diseases. More complicated, expensive and time-consuming methods are being devised in research laboratories to elucidate the precise roles of the three major determinants of deformability listed above, their importance under normal physiological conditions and how they may be specifically altered in disease states. Both of these approaches to erythrocyte deformability are necessary, since each contributes to the validity and value of the other. The direction and emphasis of basic research in this area, therefore, largely reflects feedback from the results of clinical studies wherein the usefulness of tests of erythrocyte deformability in aiding diagnosis or guiding therapy is determined.

Actual techniques used for measuring red cell deformability in vitro fall primarily into two general categories: (1) determination of the rate of movement of erythrocytes through channels with dimensions smaller than the cell diameter and (2) determination of the flow behavior of erythrocytes in suspension. The former category includes the micropipette and filtration methods and is considered to be relevant to the movement of erythrocytes through capillaries and through the naturally-occurring pores in the bone marrow and spleen. The latter category includes the majority of viscometric techniques, using either whole blood or erythrocyte suspensions in artificial media.

Micropipette Methods

The smallest micropipettes, with inside diameters of less than 1 micron, are used primarily to study the properties of the erythrocyte membrane. This is usually accomplished by measuring the pressure necessary to suck a small hemispherical portion of the membrane into the lumen of the pipette (Figure 1A). The entire procedure is performed under direct microscopic observation and requires a strictly controlled environment, precise pressure-measuring equipment and a skilled and patient investigator. Although the data obtained allow calculation of the elastic, viscous and bending moduli of the red cell membrane, the small number of cells that can be examined in this fashion preclude the use of this method for any type of screening procedure.

Larger micropipettes (greater than 3 micra in diameter) can be used for the study of overall cell deformability (a function of membrane properties, geometry and internal viscosity) by determining the pressure necessary to pull the entire cell into the pipette (Figure 1B). Again, this method is tedious

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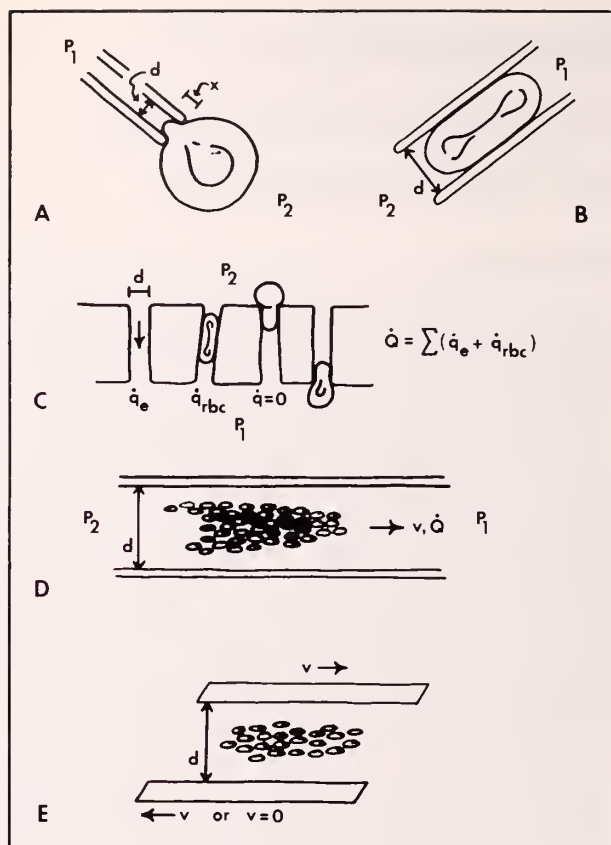


Fig. 1. Schematic comparison of methods for assessing erythrocyte deformability. The basic measurements of flow (Q), pressure (P), velocity (v) and distance (d) necessary for each are indicated. In all cases, P_2 is greater than P_1 and the direction of movement is indicated by arrows. A. Direct measurement of membrane deformability using small (less than 1 micron) pipettes. The elastic, tensile or bending properties of the membrane can be calculated from basic measurements of the excursion (x) of a portion of the cell into a pipette of diameter, d , under the influence of a pressure gradient P_2-P_1 . B. Measurement of overall cell deformability using larger (2.5-3.0 micra) pipettes. The pressure gradient necessary to pull the entire cell into the pipette is recorded. C. Filtration measurements. Flow is from top to bottom through a membrane with pores of diameter, d . The total flow through the membrane, Q , is the sum of the flow of fluid through empty pores (q_e), the flow rate of erythrocytes through the pores (q_{rbc}) and the flow rate through plugged pores ($q=0$). D. Capillary viscometry. Shear stress in this system is a function of the pressure gradient, tube diameter and tube length; shear rate is a function of tube diameter and velocity of flow. Viscosity, the ratio of shear stress to shear rate, can, therefore, be easily calculated from relatively simple measurements. E. Other viscometric methods. These depend on subjecting a cell suspension to shearing forces between a stationary surface ($v=0$) and a moving one, separated by a distance, d . Alternatively, both surfaces can be moving at the same time at the same velocity in opposite directions. The surfaces can be conical, flat or cylindrical. Knowledge of the configuration and precise dimensions of the system and measurement of the frictional drag produced by the presence of the cell suspension allows calculation of the suspension viscosity.

and characterizes only a small number of cells from a given blood sample.

Measurement of the electrical resistance between the interior of the pipette and the saline solution bathing it provides another method for assessing red cell deformability. As a red cell enters and traverses

the narrow portion of the pipette, the measured resistance will be increased over that measured when no cell is present. The duration of the elevated resistance reflects the time needed for the cell to pass through the pipette. Using this method, the application of a small, constant negative pressure sufficient to draw the cells from a suspension sequentially through a pipette allows the calculation of a mean passage time for a population of cells or the construction of a histogram indicating the frequency distribution of passage times for that cell population. This technique has the advantage of allowing measurements on a large number of cells while preserving the individuality of each measurement. However, as in all micropipette techniques involving aspiration of the entire cell into the pipette, an *overall* deformability is obtained that reflects a combination of all contributing factors. The effect of any particular factor, such as cell membrane properties, is difficult if not impossible to isolate.

Filtration Methods

Most filtration methods, especially those involving polycarbonate sieves with cylindrical channels, are similar in concept to those involving the larger micropipettes. The same factors or combination of factors determine the rate of passage of cells through either pipettes or pores in a filter, since a filter is merely equivalent to many micropipettes arranged in parallel (Figure 1C). The use of filtration techniques eliminates the ability to measure any index of individual cell behavior but has the great advantage of being technically much easier. Under the proper combination of pressures and flow rates, filtration methods may allow the calculation of the percentage or number of non-deformable cells in a blood sample or erythrocyte suspension. This is accomplished by observing changes in flow rate or flow resistance or by counting the number of plugged pores following passage through the filter of a given volume of cell suspension of known concentration. The latter method depends on the use of scanning electron microscopy to observe cells plugging the holes of the filter.

Filtration methods show the most potential as screening methods for the clinical laboratory. But care must be taken to perform enough control measurements to appreciate the assets and limitations of the particular method chosen. Also, like micropipette measurements, most filtration methods do not shed much light on the possible mechanisms of any observed abnormalities in filtration time, since all three of the major determinants of erythrocyte deformability contribute to the measurement.

Viscometric Methods

Conceptually, the next step up in scale from micropipettes and cylindrical pores in studying erythrocyte deformability is the use of capillary viscometry to study the viscous behavior of erythrocyte suspensions. The capillary tubes in these devices are of varying diameters, usually much

greater than the diameter of the erythrocyte (Figure 1D). For washed red cell suspensions in artificial media, capillary viscometry (1) demonstrates the degree of deformation of erythrocytes at various shear rates (shear deformation), and (2) allows determination of the contribution of erythrocyte internal viscosity to the suspension viscosity as measured at high shear rates. When whole blood is studied, the dependency of viscosity on shear rate is also an indication of the degree of aggregation of erythrocytes into rouleaux or larger clumps, the result of the interaction of plasma proteins and the red cell membrane. Erythrocyte suspensions can be studied at any combination of shear rates and cell concentrations observed in the circulation *in vivo*. Capillary viscometry results are useful primarily in examining blood flow properties in larger vessels and in determining the relative role of altered erythrocyte properties in overall blood or suspension viscosity.

The contribution of erythrocyte deformability to overall viscosity may also be investigated using viscometers of other types where blood samples or cell suspensions are subjected to shear forces between a conical and a planar surface (cone-plate viscometer), between two conical surfaces or between two co-axial cylinders (Figure 1E). Here the relationship of the *in vitro* situation to vascular anatomy and *in vivo* geometry is less obvious but valid and detailed analyses of blood flow properties have been carried out using such instruments over a wide range of experimental conditions. Such work has formed the basis for much of the current understanding of those factors affecting erythrocyte deformation.

A marriage of the macroscopic and microscopic approaches has been recently accomplished with the advent of new viscometers which utilize whole blood or erythrocyte suspensions but allow continuous observation of single cells or groups of cells for a visual analysis of flow deformation. Two major types of such instruments are presently in use. The first utilizes a tracking camera to follow individual erythrocytes moving through very narrow and very long capillary tubes with diameters in the same range as those used for the micropipette measurements. The second involves observation of erythrocytes in suspension subjected to shear forces between two discs rotating in opposite directions at equal speeds. This instrument is both a true viscometer useful for determining overall behavior of cell suspensions or blood samples and a sensitive microscopic device for observing, photographing and quantifying the deformation of individual erythrocytes under various conditions.

In Vivo Methods

Direct observation and measurement of erythrocyte deformation *in vivo* is limited by the inaccessibility of most vascular beds. Exceptions in humans are the conjunctival and retinal vessels and the capillaries of the nail-fold which are often used as indicators of microvascular flow patterns in human

diseases. Other species have specialized anatomical structures which allow direct observation of intact living microvasculature; examples are bat wings, frog interdigital webs and hamster cheek pouches. Other vascular beds can be examined in experimental animals following exteriorization of the tissue involved, such as the mesenteric circulation of rats, cats or dogs, and the vessels of thin muscles such as the rat gastrocnemius or cremaster. Implantable chambers allowing direct observation of the blood flow in a thin layer of connective tissue are also very useful and have been inserted into rabbit ears, the dorsal skin of rats and even into forearm skin flaps of human volunteers. In all of these preparations, erythrocyte velocity and deformability and blood viscosity in arterioles and capillary beds can be determined by analysis of videotape images or by the use of high-speed cinematography. Erythrocytes can be altered *in vivo* by drugs, diet or environmental manipulations and, in the case of experimental animals, by removal of red cells, treatment *in vitro*, and reinfusion. The behavior of these abnormal erythrocytes in the living microcirculation can then be carefully observed and recorded.

Erythrocyte Deformability Research at the Maine Medical Center

Established research techniques for assessing erythrocyte deformability in the Department of Research at the Maine Medical Center include examples from nearly all of the areas listed above. Important findings concerning the effects of oral contraceptive agents on red cell deformability using the micropipette technique served as the stimulus for a recent publication concerning the effects of methylprednisolone on erythrocyte deformability.¹ Pioneering work on the determinants of normal viscosity values for human whole blood using a cone-plate viscometer include studies on the effects of hematocrit, shear rate and temperature,² as well as pH,³ osmolality⁴ and plasma viscosity and erythrocyte aggregation.⁵

For *in vivo* observation of erythrocyte deformation, a chronically implantable rabbit ear chamber was developed⁶ which allows microscopic observation and recording of red cell behavior in small vessels in an awake and unanesthetized animal. These chambers are of an original design and are manufactured and implanted by members of the Department of Research. A major new piece of equipment was recently purchased which measures erythrocyte velocity profiles in video images of microvessels and which will be used to quantitate changes in microvascular flow patterns or rates in rabbit ear chambers due to alterations in erythrocyte deformability.

New techniques designed to measure the separate influences contributing to overall deformability are currently being applied to studies of erythrocytes from diabetics. A refinement of the filtration method⁷ allows a separation and clarification of the

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Diagnostic Imperatives In Internal Medicine

The Timely Detection of Treatable Disease

A New Series

With this issue, The JMMA begins a new series, under the arresting title of DIAGNOSTIC IMPERATIVES. This series is produced under the thoughtful guidance of Dr. Samuel Proger, Professor of Medicine, Emeritus, at Tufts University School of Medicine and President of the Bingham Fund; along with Dr. Michael Barza, Associate Professor of Medicine at Tufts University School of Medicine. Dr. Proger has been a long-time friend and benefactor of Maine medicine.

Diagnostic Imperatives in Internal Medicine will appear each month and will cover treatable diseases in: Cardiology, Gastroenterology, Dermatology, Endocrinology, Hematology, among others. The articles written by recognized authorities on the subject will be collected and later published in book form. The preface of that book will state:

"The large majority of illnesses are psychosomatic, self-limited or incurable. There is, however, a small group of diseases which stand out because they possess all the following characteristics: (1) they are curable or able to be arrested in a manner that is substantially more than palliative; (2) untreated they lead to death or severe disability; and (3) their progression in the absence of treatment occurs in a relatively short period of time."

Each article in this series is written in a straightforward, practical style, well suited to this *Journal* and is designed to alert the practicing physician to the "Timely Detection of Treatable Disease."

DFH

Some Comments on Medical Diagnosis

SAMUEL PROGER, M.D.*

The discussion of medical diagnosis that follows will concern itself with the central role of factual knowledge and experience, the process by which one reaches a diagnosis, and some of the human factors on the part of the patient and the physician that affect diagnosis. And finally, I shall consider briefly the contributions that advances in decision analysis and computer technology may make in the future.

The most important of all diagnostic considerations is that related to the recognition of conditions that must be diagnosed early if treatment is to be beneficial. Next come conditions which, whenever diagnosed, will still respond in most cases to curative therapy. Then there are the conditions which, although incurable, will, whenever diagnosed, still benefit from supportive therapy. In the chapters to follow, these diagnostic categories will be identified and expanded, but in all cases the diagnosis will be seen as important because it leads to effective treatment.

The sequence of the practitioner's development in diagnosis (and treatment and prognosis as well) consists of, first, the acquisition of knowledge from teachers, colleagues, books, and journals; second, the gaining of experience (empiric knowledge); and finally, the development of judgement. It is when this triad of information, experience, and judgement is suitably blended that the sound diagnostician emerges.

Acquiring Knowledge

The primary and basic step in diagnosis is the simple acquisition of facts, since the diagnostician must first of all be well informed.

The information that one obtains from the customary "complete" history, physical examination, and diagnostic tests, usually provides data that singly or in combination serve as a starting point for sequential hypotheses. This is an approach which assumes that a reasonable amount of basic information will provide the necessary clues for further progress toward a diagnosis. The case building strategy is in effect a process of discarding some findings while adding others until we reach a recognizable syndrome that serves to establish the final hypothesis or presumably correct diagnosis. This process is effective only to the extent that there is knowledge of what information to discard and what to add, and for what purpose. Unless we know the symptoms and findings in a patient with polymyalgia rheumatica we are not likely to direct questioning or seek data to establish the diagnosis; and the patient may lose the sight of an eye while we wonder what to do.

Then there is an approach in which one accumulates a great mass of information in the hope that, buried somewhere in this mass, one may find the diagnosis. Such an unthinking process may obscure rather than reveal critical bits of information. We need only such information, with step-like additions, that will set off a rational chain of sequential hypotheses. Each new fact has its special relevancy.

The nature of clinical expertise lies more with the

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rapid and efficient establishment of contexts or hypotheses for diagnostic evaluation than with the exhaustive pursuit of every possibility. Exhaustive and complete search is only possible in the simplest of problems. What seems far more important than completeness is the ability to recognize and act rapidly upon the available, though incomplete clues which the patient offers us. Indeed, the efficient expert in clinical medicine at times appears to have an approach that is the antithesis of an exhaustive or complete search.

To reiterate, the conventional approach to diagnosis is to collect a "reasonable" data base as a routine and to direct the search for further information as dictated by sequential hypotheses. This approach is not new. Indeed, in his famous report of 1910, Flexner in comparing the clinician's approach to problem solving with that of the scientific investigator noted that:

"The main intellectual tool of the investigator is the working hypothesis. The scientist is confronted by a definite situation, he observes it for the purpose of taking in all the facts. These suggest to him a line of action. He constructs an hypothesis. Upon this he acts, and the practical outcome of this procedure refutes, confirms or modifies his theory. Between theory and fact his mind flies like a shuttle; and theory is helpful and important just to the degree in which it enables him to understand, relate and control phenomena. This is essentially the technique of research: Wherein is it irrelevant to bedside practice? The physician too is confronted by a definite situation. He must seize its details, and only powers of observation trained in actual experimentation will enable him to do so. The patient's history, condition, symptoms form his data. Thereupon, he too, frames his working hypothesis, now called a diagnosis. It suggests a line of action. Is he right or wrong? Has he actually amassed all the significant facts? Does his working hypothesis properly put them together?"

To "amass all the significant facts" requires the continued acquisition of knowledge. The person who has an unusual capacity for storing and recalling factual knowledge, that is, the person who has a good memory, has an advantage over one who is less fortunate in this respect. All other things (such as the ability to evaluate, to connect, to apply) being equal, the best informed diagnostician is the best diagnostician. Rare diseases, exceptional variants, unusual manifestations, can only be recognized if they are known to exist.

We must however, not be guilty of encouraging answers to questions or of seeking findings to fit a prematurely suspected diagnosis. There must be an open-minded collection of facts.

Experience

The accumulation of facts must be, as I have in-

dicated, a continuing process in which the role of experience emerges as another means of acquiring knowledge. Experience gives to factual knowledge its practical meaning by placing it in perspective. Experience makes it possible to judge the relative value of facts and to apply these values to the problem of diagnosis. For example, the fourth year medical student is more likely to give greater emphasis to the consideration of a particular rare disease than is the experienced clinician. To the medical student, the unusual condition might be as common as the usual; he may have seen one example of each. His reaction is conditioned by his experience, which has been limited. Adequate experience is thus a precondition to balanced judgement, and this experience, to be meaningful, must in turn be complemented by a body of facts derived from inquisitiveness and the urge to know. The best clinician is not just the most experienced clinician. In fact, to the ignorant, experience may actually be misleading. Experience based on false premises which in the past led to the widespread practice of blood letting to remove bad humours, or vigorous purging and the massive use of colonic irrigations to eliminate toxins are historic examples. It is the wise and accurate appraisal of experience that is important.

The accumulation of experience is a process which stems from the vaguely recalled and even forgotten past to the easily recalled and sharply etched present. Since more recent experiences are generally more easily remembered, the whole of one's experience may provide an uneven impact against which one must guard. We are not evenly immersed in our experiences. It is important to make allowances accordingly.

Another circumstance that may throw experience out of perspective is the peculiar nature of one's own total experience. The surgeon's experience is of one sort, the internist's of another. To the specialist in infectious disease, unexplained fever is likely to be viewed as due to an infection, to the tumor specialist, a malignancy, to the immunologist, a "collagen" disorder. We must be sufficiently aware of our particular experience to recognize its limitations as well as its value, since no one has an all inclusive experience.

Not only is the totality of one's experience likely to be distorted by the dominance of recent events, but it is also likely to be thrown out of focus by the forceful intrusion of particularly vivid incidents. Having once witnessed the death of a member of one's family from a perforated diverticulum of the colon, it becomes difficult thereafter to realize that colon diverticula are by and large harmless. The vagaries of experience can, therefore, produce diagnostic prejudices which like other forms of prejudice may lead to illogical or irrational thinking.

With respect to experience, I might comment further about rare conditions. To be sure, if the average practitioner misses only rare diagnoses, he rarely misses diagnoses. However, he must be constantly on

guard less he miss the rare correctible condition that if not recognized and treated might prove lethal or disabling. Fortunately, there are not too many such, though they should be of particular concern to us.

Rare treatable diseases have been regarded in the past as generally beyond the diagnostic competence of family practitioners. This is no longer true. Advances in technology are expanding and will continue to expand so that the primary physician can achieve a diagnostic capability comparable in many areas to that of today's subspecialists. For example, the primary physician seeing a patient with a bizarre murmur, recurrent embolization, fever, and leukocytosis, may be guided to a diagnosis of atrial myxoma by an echocardiogram. Not too many years ago this was a diagnosis commonly overlooked even by the cardiologist and often was not made until an autopsy was performed. Also, not too many years ago even if the diagnosis were made, nothing could be done about it. Recent advances have made the diagnosis simple and curative therapy possible.

To illustrate further, in an elderly demented patient the primary physician can resort to the CT scan to establish a diagnosis of "normal" pressure occult hydrocephalus, a condition that is as important as it is rare, not only because it is curable but because if the diagnosis is missed the patient might undergo years of unnecessary institutional care. In both of the above examples, the family physician will need help in managing the patient, in the first instance from a cardiac surgeon and in the second from a neurosurgeon. But in all likelihood neither condition would have been diagnosed by the primary physician or successfully treated by the surgeon before the quite recent introduction of the technological hardware.

As technical advances in diagnosis continue, as surely they will, the diagnostic role of the primary physician will expand further. When we enter the twenty first century, the family physician as a diagnostician will be as far advanced in many areas over today's family physician as the latter is advanced over his nineteenth century general practitioner counterpart.

To be sure, technology can be exploited and its hardware overused and misused. It often is. To avoid this will require a rational approach to proper evaluation. But in time the advances find their appropriate and useful place. Primary care physicians, with their special training, and with ready access to increasingly sophisticated diagnostic tools, can become the general diagnosticians of the future.

The Human Factor: Patients

We need to understand the effects of variations in patients' personalities and organ functions on symptoms and signs. It is because of such differences in the personality and biological behavior of patients that the symptoms and signs of illness often seem so capricious, unpredictable and infinitely varied. Not only are the evidences of a particular disease dissimilar from patient to patient, but the accounts

of the symptoms are also likely to be highly diverse. There are those who have a high threshold for symptoms; they will minimize or even deny them. On the other hand, there are those with a constant overflow of disturbing sensations, many of which are unrelated to recognizable disease. Some patients are voluble, some laconic. The close-mouthed patient may give the questioner only what is demanded, the agreeable patient may give what he or she thinks the questioner wants, the loquacious assertive patient what he or she thinks the examiner should have. Some patients come quickly to the point, others circumnavigate it. Some confuse, others clarify. The physician's questions may be parried by irrelevant interjections which are likely to take the interviewer far afield. On the other hand, an occasional irrelevant chance remark by a patient may provide the essential clue to a diagnosis. The examiner must learn to weave his way through such distortions. The basic difficulty, I suppose, is that human beings so often seem to be irrational, and their behavior quixotic. There is a certain identifiable limit to logical responses. There is no limit to illogical ones.

The Human Factor: Physicians

The diagnostic process touches on many human qualities of the physician. There are some who have a greater capacity than others for reasoning, both deductive and inductive. There are some who require for intellectual support dogmatic instruction; they prefer to believe rather than to comprehend. Others incline more to skepticism. There are some more imaginative than others; and some with more sensitive intuitions. There are some with better memories; others with more industry and persistence. Then there are modifying attributes of temperament such as cautiousness, pride, stubbornness, and carelessness. In short, all those human qualities that distinguish one person's behavior from another are combined in that complex intellectual process that finally leads to an appropriate diagnosis.

I say "appropriate" rather than correct. For suppose one were faced with a situation in which a definite diagnosis is not possible; however the more likely diagnosis from the point of view of pure logic would be distressing to the patient but favorable to the clinician's reputation and self-esteem, while the less likely diagnosis would result in no harm, and would in addition contribute to the patient's peace of mind. In such a situation it is more humane and hence, in a qualified sense, more appropriate to choose the less likely diagnosis. A consideration of the differential diagnosis of multiple sclerosis and psychoneurosis is an example.

There are physicians who find it difficult to say they don't know. After collecting all the information they consider pertinent, they insist on cramming the data into a diagnostic category whether or not it fits. If it doesn't fit, it is simply viewed as atypical. We must bear in mind that unless we assume that every conceivable syndrome has already been described, we are from time to time seeing syndromes as yet

unrecognized. The condition now known as McArdle's syndrome, for example, might, before McArdle's report, have been diagnosed atypical intermittent claudication. Before Herrick's report almost 70 years ago, patients with acute myocardial infarction were simply viewed as having atypical angina pectoris or status anginosus. And so it goes.

In arriving at a diagnosis, we should recognize the effect of the physician's emotional reaction to a patient. I was once told by a psychiatrist that if, after seeing a patient, he felt dispirited and heavy hearted, he thought he was probably dealing with a depression;—if he felt irritated and bothered, a psycho-neurosis;—if he felt confused, a schizophrenia. In this example the physician's reaction was helpful diagnostically. At other times it can be detrimental.

Then there are the effects of fatigue, of personal interests and enthusiasms, of the amount of time available, of a preoccupation with other problems, and so on. It is the proper weighing and the subtle interplay of a host of intellectual, psychological, and even moral and ethical factors that determine that elusive quality known as good judgement, which, in turn, results in sound diagnoses.

The Future

I have attempted to describe some of the circumstances and factors, especially human factors (often unsuspected), that are involved in the diagnostic process as we have applied it in the past. But what about the future? What about computers and advances in techniques of decision-making that promise to provide us with a more logical use of available information?

As to computers, let me say at the outset that we must guard against a common human tendency to resent the intrusion of anything new. For the new disrupts a comfortable and familiar pattern and hence is disconcerting. This has always been true. When Laennec introduced the stethoscope over 150 years ago, he was accused of being too enthralled with mechanical gadgets. The gadget interposed itself between the physician and the patient and therefore made the relationship of the patient to the physician too impersonal. The fact is, we are better prepared to resist change than to adopt it.

The computer may in time add immensely to our ability to manipulate information in arriving at a decision; it may be able to absorb much of the effort of the clinician. It is, however, largely a deductive and not an inductive instrument. Also, its general disadvantages are to some extent similar to those of the mind. It can only work with what it is given. A principal handicap to the computer approach will always be the peculiarly human differences in patients' responses to illness and the limitless variations in their accounts of what troubles them.

Though the computer may have a place in the future, it will not eliminate the need for thinking, and particularly for feeling and creative human beings. It will simply add a new dimension to this need.

Promoting logical thinking is what the current in-

terest in decision analysis is all about. As medicine becomes more complex, there will be more opportunities for sloppy thinking and it will become easier and more dangerous to fall into bad thinking habits. Diagnosis is after all simply a decision-making process. Advances in techniques of decision making are indeed promising and they are likely to eliminate much of the looseness and uncertainty that are so widespread in the approach to clinical diagnosis today. A wider knowledge of the nature of probabilities must result in a more rational application of information. We can look forward to important advances in this area.

GENERAL COMMENT

We are told that "we see what we look for; we look for what we know." And, I might add, we know best what we see most. However, among the diagnostic imperatives are relatively uncommon conditions. To the maxim therefore, one should add that we must sensitize ourselves to recognize those rare diseases which, if not diagnosed and treated early may lead to disability or death.

The general principles that I have been discussing apply to all diagnoses. But as indicated at the outset, diagnoses are variously important. Most will, in the very nature of things prove less important since they relate to illness that is either self-limited or incurable. In these conditions, the passage of time will make the diagnosis either obvious or irrelevant. There are however, diagnoses that are very important because they lead to therapeutic measures without which the patient may die needlessly or suffer preventable disability. Many of these conditions are seen by primary care physicians and in an ambulatory setting because the symptoms often appear to be minor or unimportant and the illness rather nebulous and ill defined. For example, in a patient with unrecognized early evidence of pernicious anemia, slight glossitis with some soreness of the tongue may seem a rather minor annoyance, and the diagnosis unimportant. However, at this stage, though difficult to diagnose, pernicious anemia is easy to treat effectively. The apparently trivial symptom is anything but trivial. For if allowed to progress undiagnosed and untreated, serious incapacity from gross neurologic damage might result. Herein lies a major diagnostic challenge, namely to separate the truly trivial symptoms of a minor and self-limited illness from the early similar symptoms that herald the onset of a major curable disease.

Probably the most difficult of all diagnostic challenges is the recognition of the insidious onset of a serious correctable disorder whose symptoms are submerged in a welter of psycho-somatic complaints. This is a situation that demands superior diagnostic skills.

What is known about the benefits of early diagnosis in remedial diseases is already in the collective minds of clinicians, but has not been

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From the Secretary's Notebook

Summary of 1979 Fall Meeting of the M.M.A. House of Delegates November 17, 1979 at Waterville, Maine

The Fall Meeting of the M.M.A. House of Delegates was held at the Mid-Maine Medical Center (Thayer Unit) in Waterville on Saturday, November 17, 1979, with an attendance of 56 delegates and alternates, and three guests. Brinton T. Darlington, M.D., President of the M.M.A. called the meeting to order and George W. Bostwick, M.D., Speaker of the House, presided.

1. Reports of Officers—Dr. Darlington, President, asked for a moment of silence in memory of the recent passing of two former Presidents of the M.M.A., Drs. Asa Adams and Charles Branch.

It was announced that the M.M.A. had recently hired new **legal counsel**—Gordon H. Smith of Sanborn, Moreshead, Schade & Dawson of Augusta.

It was reported that **Medical Mutual Insurance Company** of Maine recently reimbursed the M.M.A. \$12,474.10 that was given in seed money to help start the company.

Members were invited and encouraged to pay their 1980 State and County **dues** early.

2. Committee Reports

a) *Health Care Financing*—Dr. Harry Bliss, Chairman, and Dr. Peter Shrier, Chairman of the subcommittee on negotiations, reported on activities over the past 18 months, specifically in regard to its discussions with Blue Shield relative to a new contract. Mr. Frank Stred, Executive Director of the M.M.A., reported also on his involvement in the negotiations since February. Dr. Bliss presented a resolution from his committee which was rejected. The following resolution was submitted, amended and approved:

WHEREAS The Maine Medical Association desires to avoid a relationship with Blue Shield of Maine which might be considered improper or illegal by either the courts or a regulatory agency and,

WHEREAS it desires to respond to the request by Blue Shield that the Association give up the power of approval over new policies and plans, which power has been an integral part of the Agreement since the physicians first agreed to underwrite the financial stability of Blue Shield (the Physicians Service Plan) when they initiated the program and

WHEREAS the Association wishes to maintain an even-handed relationship with other health insurance companies and

WHEREAS the Association is concerned for the continuing relationship with all third-party providers and with the rising cost of operation of a large Health Care Finance Committee meeting on a regular basis as a policy making, analysis and review group and

WHEREAS the need for physician subsidy of the Blue Shield plan has ended and Blue Shield has financial reserves in excess of \$4.5 million and

WHEREAS the Association takes no position whatsoever on whether or not an individual physician should participate in any particular insurance plan.

NOW, THEREFORE, BE IT RESOLVED that the Maine Medical Association hereby authorizes the Executive Committee and the Health Care Finance Committee to maintain a continuing relationship with Blue Shield of Maine, that relationship to be consistent with and the same as the existing relationship between the Maine Medical Association and all other health insurance carriers,

That the Maine Medical Association authorizes the Executive Committee and the Health Care Finance Committee to provide to Blue Cross and Blue Shield all information, commentary and review services which are provided to all other health insurance carriers and are permitted under existing State and Federal statutes and regulations,

That the Maine Medical Association directs the Executive Committee and the Health Care Finance Committee to withdraw approval of all existing Blue Shield subscriber agreements and to refrain from endorsing any health insurance contract whether proposed by Blue Cross/Blue Shield or any other health insurance carrier,

Furthermore, that the Maine Medical Association directs the Executive Committee and the Health Care Finance Committee to refrain from negotiations regarding physician fee schedules in any health insurance contract,

Furthermore, Be It Resolved that none of the above directives is to be construed as prohibiting existing or future negotiations with State and Federal agencies or their intermediaries.

b) *Nominations*—Dr. Francis I. Kittredge, Chairman, presented nominees for election to the Executive Committee, to serve from January 1, 1980 until the Annual Meeting in June 1980, and they were **approved** as follows:

Oxford—David L. Phillips, M.D.
Penobscot—Patrick W. Kamm, M.D.
Somerset—Richard C. Taylor, M.D.
Waldo—Harold E. Knuuti, M.D.

No nominees were forthcoming from Hancock or Lincoln-Sagadahoc Counties.

c) *School Health*—It was announced that this committee will be seeking representatives from each county medical society to serve as members for the coming year.

d) *Subcommittee on M.M.A. Health Insurance Plan*—Dr. Michael Rynne, Chairman, reported that

his committee will be studying various options over the next few months and expects to have a report for the House of Delegates at its Spring 1980 meeting.

3. **New Business**—Dr. Robert McAfee, **AMA Delegate**, reported on various subjects that will come before the AMA House at its meeting later this month, and its Annual Meeting next summer. He encouraged any member to call him directly regarding their views on any issue that will be discussed.

4. Adjourned at 4:00 P.M.

PATRICIA A. BERGERON
Secretary-Treasurer, M.M.A.

ERYTHROCYTE DEFORMABILITY: THE DETERMINATION OF ITS IMPORTANCE AND THE IMPORTANCE OF ITS DETERMINATION—Continued from Page 15

degree to which red cell geometry (size, shape, surface area-to-volume ratio) and internal viscosity (hemoglobin concentration, presence of nucleus in erythrocyte precursors) influence passage of the cells through cylindrical channels. A sensitive capillary viscometer, again designed and built by the Research staff at MMC, provides shear stresses and shear rates comparable to those seen in any point of the circulation and the contributions of erythrocyte internal viscosity and shear deformation (related to geometry) can be elucidated and compared to the results from filtration tests. The newest method, which shows considerable promise, measures the rate of migration of red cells subjected to a centrifugal force; this rate is a function of cell shape, deformation and density, as well as the density and viscosity of the suspending medium. The appropriate use of one or more of these new methods in conjunction with other established techniques provides a multi-faceted experimental approach to the assessment of the physical properties of abnormal erythrocytes and their contribution to disease processes.

The ultimate aim of this research into erythrocyte deformability being performed at the Maine Medical

Center is two-fold: (1) to characterize those properties of erythrocytes which determine overall deformability in health and disease and (2) to develop clinically applicable methods of measuring red cell deformability that not only identify abnormalities in erythrocyte physical properties but also suggest possible areas of therapeutic intervention.

REFERENCES

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2. Rand, P.W., Lacombe, E., Hunt, H.E., and Austin, W.H.: Viscosity of normal human blood under normothermic and hypothermic conditions. *J Appl Physiol*, 19:117-122, 1964.
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4. Rand, P.W., and Lacombe, E.: Hemodilution, tonicity, and blood viscosity. *J Clin Invest*, 43:2214-2226, 1970.
5. Rand, P.W., Barker, N., and Lacombe, E.: Effects of plasma viscosity and aggregation on whole-blood viscosity. *Amer J Physiol*, 218:681-688, 1970.
6. Rand, P.W., Wilkinson, A.F., Lacombe, E., and Barker, N.: An electrode-containing rabbit ear chamber for microvascular measurements. *Microvasc Res*, 2:508-519, 1970.
7. Norton, J.M., Barker, N.D., and Rand, P.W.: Determination of a relative filtration time for dilute erythrocyte suspensions: Contribution of internal viscosity and surface area-to-volume ratio. In preparation.

DIAGNOSTIC IMPERATIVES IN INTERNAL MEDICINE—Continued from Page 19

brought into focus, assembled and organized in the most useful way. What follows in the subsequent chapters is an attempt to do just that.

REFERENCE

- Flexner, A.: Medical education in the United States and Canada, Bulletin No. 4. The Carnegie Foundation for the Advancement of Teaching. Boston, Merrymount Press, 1910.



COMMITTEE FIGHTS HEALTH CARE COSTS

As a part of its efforts to keep health care costs down, the Cost Containment Committee at Blue Cross and Blue Shield of Maine has agreed to support two new programs:

Hypertension Control

The first is a worksite hypertension control program in the Lewiston/Auburn area. Impetus for this came from the Maine Labor Group on Health and the Maine High Blood Pressure Council. Approximately 4,000 employees from various industries in the area will be screened for high blood pressure. Companies with 400-600 employees will be chosen on the basis of their willingness to participate and pay a per capita screening fee.

The program will consist of a six-month period of screening, family physician referral, and follow-up, which will be performed by nurses of the Androscoggin Home Health Services, Inc. One year later, a re-screening and evaluation of data will be performed.

The Blue Cross and Blue Shield Associations have stated that a successful hypertension screening program prevents one disabling event (such as heart disease, stroke, or kidney failure), in every 25 hypertensive workers. The cost of such an event, including hospital and surgical services, physician fees and disability days, has been calculated to be about \$15,000.

Poison Control

The other program sponsored by Blue Cross and Blue Shield of Maine involves a \$20,000 grant to the Poison Control Center at Maine Medical Center in Portland. This grant will help the center maintain its statewide program as well as help alleviate expenses for inappropriate emergency room visits.

Dr. Frank Lawrence, director of the Poison Control Center, estimates that nearly 65% of all poison cases can be effectively treated in the home using the center's recommendations and call-back procedure. The problem, as he sees it, is that only about one-half of the people in Maine are aware of the center's existence.

When a poison victim needs help, the center offers a "hotline" which gives immediate on-the-spot assistance. Via a toll-free telephone number (1-800-442-6305, or in Portland 871-2381) the general public receives free, professional treatment instructions for more than 250,000 commercial products, pesticides, and plants on a 24-hours-a-day, 7-days-a-week basis.

In addition to offering a hotline, the Poison Control Center has a public awareness program, aimed at informing the general public about common toxic household and commercial products, and at keeping medical professionals up-to-date on poison treatment material.

Physician Gets Award

Other action by the Cost Containment Committee includes a \$100 award given to Clement A. Hiebert, M.D. of South Windham, for his idea on how to help save money on health care expenses. Dr. Hiebert, who specializes in thoracic/cardiovascular surgery, suggested that physicians be made aware of the cost of various procedures, tests and drugs at the time they order them. This could be done by having physicians receive copies of each patient's bill, or by physicians having a price sheet of all common procedures, tests, and drugs they order.

The Cost Containment Committee consists of Blue Cross and Blue Shield staff and Board members, and solicits ideas and projects from all segments of the community, supporting (and awarding) those with potential for lowering health care costs.



CONTINUING MEDICAL EDUCATION IN MAINE

Conferences and Workshops

Title: Diabetes Update
Date: March 29, 1980
Location: A.R. Gould Memorial Hospital, Presque Isle
Sponsors: Aroostook County Regional Medical Standards Committee (PSRO); A.R. Gould Memorial Hospital, and Medical Care Development
Credit: AMA Category I—6 hours
Reg. Fee: To be determined
 For further information contact Gerald Gould, Medical Care Development; 622-7566.

Hospital Activities

Augusta General Hospital Augusta, Maine

Jan. 22, 1980 **Tumor Conference**
 7:30-8:30 a.m. Faculty to be announced
 Jan. 29, 1980 **Hypertension (Newer Rx?)**
 7:30-8:30 a.m. Paul Parker, M.D., Maine Medical Center
 Feb. 25, 1980 **A Microbiologic Approach to Infections in the Abdomen**
 7:30-8:30 a.m. David R. Ginder, M.D., Mid-Maine Medical Center

These programs have been certified AMA Category I and AAFP (prescribed). For further information contact Mrs. Nancy Favorite; 623-4711. These programs may be viewed over ITS.

Augusta Mental Health Institute Augusta, Maine

Every other **Grand Rounds**
 Thurs. Augusta Mental Health Institute
 The 10-11:30 a.m. sessions are Grand Rounds; the 1:30-3 p.m. sessions are Inpatient Psychiatry Courses. All programs have been certified AMA Category I. For further information contact Pauline H. Soper; 622-3751.

Eastern Maine Medical Center Bangor, Maine

Every Mon.	EEG Conference	12-1 p.m.
Every Mon.	Surgical Service—Chief's Rounds	5-6 p.m.
4th Mon.	ENT Section Meeting	12-1 p.m.
4th Mon.	Neurosurgery Section Meetings	4-5 p.m.
3rd Tues.	Dermatology-Pathology Conference	5-6 p.m.
3rd Tues.	Dermatology Section Meeting	6-7 p.m.
4th Tues.	Pulmonary Medicine Section Meeting	8-9 a.m.
1st Wed.	Hematology/Oncology Meeting	8-9 a.m.
Every Wed.	Tumor Clinic Conference	2-5 p.m.
Every Wed.	Radiology Conference	5-6 p.m.
	(1) Ultrasound/Nuclear Medicine	

	(2) Radiology Film Review	
	(3) Neuroradiology	
	(4) Teaching File Conference	
1st Thurs.	Ophthalmology Section Meeting	7:30-8:30 a.m.
	OB-GYN Conference	8-9 a.m.
	(1) Pathology	
	(2) GYN Analysis	
	(3) OB-Pediatric Combined	
	(4) In-Service and Education	
Every Thurs.	Pediatric Grand Rounds	9-10 a.m.
Every Thurs.	Medical Service Conference	10-11 a.m.
Every Thurs.	Cardiology Conference	11 a.m.-1 p.m.
2nd Thurs.	Orthopedic Grand Rounds	7:45-8:45 a.m.
4th Thurs.	Orthopedic Service Meeting	7:30-9 a.m.
4th Thurs.	Surgical Service Death Review	7:45-8:45 a.m.
Every Thurs.	Psychiatric Service Grand Rounds	10-11 a.m.
4th Thurs.	Urology Section Conference	7:30-8:30 a.m.
Every Fri.	Neurology Grand Rounds	8-9 a.m.

Visiting Professor Program:

2nd Thurs.	Medical Service Visiting Professor	10 a.m.-5 p.m.
2nd Thurs.	Anesthesia Service Visiting Professor	7-8 a.m.
3rd Thurs.	OB/GYN Service Visiting Professor	10 a.m.-4 p.m.
Saturdays	Surgery Service Visiting Professor	8 a.m.-Noon
4th Thurs.	Pediatric Service Visiting Professor	10 a.m.-5 p.m.
as scheduled	Orthopedic Service Visiting Professor	
as scheduled	Family Practice Visiting Professor	
as scheduled	Psychiatric Service Visiting Professor	
as scheduled	Radiology Service Visiting Professor	

All activities have been certified AMA Category I. For further information contact James F. Lawsing, III, M.D., Coordinator, Medical Education; 947-3711 Ext. 330.

Henrietta D. Goodall Hospital Sanford, Maine

Jan. 22, 1980 **Peripheral Vascular Disease**
 Saul Katz, M.D., Maine Medical Center
 Feb. 26, 1980 **What's New in Endocrinology**
 David Slovick, M.D., Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts
 These meetings will be held at the Henrietta D. Goodall Hospital's Conference Room at 7 p.m. These programs have been certified AMA Category I and AAFP (prescribed). For further information contact Melvin Bacon, M.D.; 324-3632.

A. R. Gould Memorial Hospital Presque Isle, Maine

Feb. 11, 1980 **SUO and Chronic Infections**

7:30 p.m. Frank Tally, M.D., Tufts University School of Medicine, Boston, Massachusetts

This meeting will be held at the Rotary Regional Educational Center at the A. R. Gould Memorial Hospital. This program has been certified AMA Category I. For further information contact Marilyn Dean; 769-2511.

Maine Medical Center Portland, Maine

Every Mon.	Student Technologist Conference	8 a.m.
Every Mon.	Hematology-Pathology Conference	11 a.m.
Every Mon.	Pulmonary Conference	12 Noon
Every Mon.	Pediatric Residents' Conference	1 p.m.
Every Mon.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Mon.	Surgical Pathology Review	4 p.m.
Every Mon.	Radiology Journal Club	5 p.m.
1st &	Clinical Nephrology Conference	11 a.m.
3rd Mon.		
1st &	Hematology-Pathology Conference	12 Noon
3rd Mon.		
3rd Mon.	Eye Conference	11:45 a.m.
Every Tues.	Radiology Residents' Seminar	7 a.m.
Every Tues.	Family Practice Grand Rounds	9 a.m.
Every Tues.	Electrocardiographic Interpretation	1 p.m.
Every Tues.	Psychiatric Grand Rounds	1:30 p.m.
Every Tues.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Tues.	Surgical Seminar	4 p.m.
Every Tues.	Pathology Slide Seminar	4 p.m.
1st &	Radiology-Pathology Conference	12 Noon
3rd Tues.		
1st &	Neurology Conference	12 Noon
4th Tues.		
2nd Tues.	Infectious Disease Conference	12 Noon
3rd Tues.	Hematology Conference	12 Noon
5th Tues.	Oncology Conference	12 Noon
Every Wed.	Radiation Therapy Conference	7 a.m.
Every Wed.	Urology Conference	7 a.m.
Every Wed.	Student Technologist Conference	8 a.m.
Every Wed.	Continuing Education Seminar	8 a.m.
Every Wed.	Medical Conference	9 a.m.
Every Wed.	Psychiatric Journal Club	12 Noon
Every Wed.	Cardiology Seminar	12 Noon
Every Wed.	Surgical Grand Rounds	5 p.m.
2nd Wed.	Guest Internist—Medical Conference	9 a.m.
4th Wed.	Medical Mortality Conference	9 a.m.
Alt. Wed.	Neurology-Psychiatry Seminar	11 a.m.
Alt. Wed.	Anesthesiology Journal Club	3 p.m.
Every Thurs.	Thoracic Surgery Conference	7 a.m.
Every Thurs.	OB/GYN Conference	7 a.m.
Every Thurs.	Anesthesiology Clinical Conference	7 a.m.
Every Thurs.	Diagnostic Radiology Teaching Conference	7 a.m.
Every Thurs.	Surgical Conference	8 a.m.
Every Thurs.	Pediatric Conference	9 a.m.
Every Thurs.	Tumor Consultation Board	11 a.m.
Every Thurs.	Medical Residents' Conference	12 Noon
Every Thurs.	Surgical Seminar	4 p.m.
Every Thurs.	Endocrinology Conference	5 p.m.
Every Thurs.	Dental Specialty Lecture	6 p.m.
1st Thurs.	Anesthesia Mortality Conference	7 a.m.
1st Thurs.	Guest Pediatrician	9 a.m.
1st Thurs.	Gastroenterology Conference	12 Noon
1st &	Cardiac-Surgical Conference	12:30 p.m.
3rd Thurs.		
1st, 3rd, &	Pulmonary-Physiology Conference	12:30 p.m.
5th Thurs.		

2nd Thurs.	Cardiology Teaching Conference	12:30 p.m.
2nd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
2nd Thurs.	Eye Staff Scientific Session	5:30 p.m.
2nd Thurs.	Maine Medical Center Medical Staff Meeting and Scientific Session	6 p.m.
2nd &	Pulmonary-Pathology Conference	12 Noon
4th Thurs.		
2nd &	Endocrinology Conference	12 Noon
4th Thurs.		
3rd Thurs.	Combined Guest Physician or Guest Surgeon Program	8 a.m.
3rd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
4th Thurs.	Surgical Mortality Conference	8 a.m.
4th Thurs.	Anesthesia Mortality Conference	3:30 p.m.
Last Thurs.	Pediatric Mortality Conference	9 a.m.
Every Fri.	Thoracic-Surgical Conference	7 a.m.
Every Fri.	Nuclear Medicine Conference	7 a.m.
Every Fri.	Student Technologist Conference	8 a.m.
Every Fri.	Neurological-Neurosurgical Conference	8:30 a.m.
Every Fri.	Gastroenterology Conference	9 a.m.
Every Fri.	Medical Rehabilitation Staff Conf.	9 a.m.
Every Fri.	Orthopedic Conference	9 a.m.
1st Fri.	Dermatology Conference	12 Noon
2nd Fri.	Nephrology Conference	12 Noon
3rd Fri.	Rheumatology Conference	12 Noon
4th Fri.	Oncology Conference	12 Noon
Alt. Fri.	Oncology Radiation Conference	7 a.m.
Alt. Fri.	Gastroenterology Conference	10 a.m.
All programs have been certified AMA Category I. For further information contact Costas T. Lambrew, M.D.; 871-2111		

Mercy Hospital Portland, Maine

Feb. 7, 1980 **Antibiotic Use in Normal & Abnormal Renal Function**
7 p.m. Andrew Whelton, M.D., Associate Professor of Medicine, Johns Hopkins University
This program will be held in the Mercy Hospital auditorium and has been certified AMA Category I. For further information contact Gwen Gray; 774-1461.

Mid-Maine Medical Center Waterville, Maine

Jan. 22, 1980 **Thyroid Disease in Pregnancy**
CASE PRESENTATION—Ann Dorney, M.D., Mid-Maine Medical Center
DISCUSSION—Herbert Bartholomew, M.D., Augusta General Hospital
Jan. 24, 1980 To be Announced
Jan. 29, 1980 **Hypertension in Pregnancy**
CASE PRESENTATION—Sanders Burstein, M.D., Mid-Maine Medical Center
DISCUSSION—Speaker to be announced
Jan. 31, 1980 **Drug Therapy in the Elderly**
H. Wayne Tobin, M.D., Mid-Maine Medical Center
Feb. 7, 1980 **Parenteral Nutrition**
Irvin L. Paradis, M.D., Mid-Maine Medical Center
Feb. 14, 1980 **A Case Presentation**
Central Maine Family Practice Residents
All programs are being held at Mid-Maine Medical Center in the South Wing Conference Room from 12-1 p.m. and have been certified AMA

Continued on Page 28

Necrologies

DONALD COULTON, M.D.

1918-1979

Dr. Donald Coulton, 61, of Bangor, Maine died unexpectedly at a local hospital on March 31, 1979.

Born in Milford, Connecticut on January 1, 1918, he was the son of Homer and Irene Coulton.

He was graduated from Williams College and received his medical degree from Harvard Medical School in 1943. Dr. Coulton interned at the Hartford Hospital in Connecticut and served residencies at the Massachusetts Memorial Hospital, the Boston Lying-In Hospital and the Free Hospital for Women.

Dr. Coulton moved to Bangor in 1947, where he opened a practice in obstetrics and gynecology, and joined the Eastern Maine Medical Center's staff. He limited his practice to gynecology at the St. Joseph Hospital. Dr. Coulton was immediate past president of the St. Joseph Hospital staff, a former member of the board of trustees, and medical committee executive staff. He was also a gynecological and surgical consultant at the Seabasticook Valley Hospital, the Greenville and Dexter hospitals, the former Dow AFB Hospital and the Cutler Health Center, University of Maine.

Dr. Coulton was a member of the Penobscot County Medical Society, the Maine Medical Association and the American Medical Association. He was also a past president and international lecturer of the American Society of Clinical Hypnosis, and Fellow of the American College of Obstetrics and Gynecology.

Surviving besides his mother of Milford, Connecticut and Bangor, are his widow, Eleanor Coulton of Bangor; one daughter, Mrs. Benjamin Haskell of Brewer; one son, Peter S. Coulton of Bangor; and three grandchildren.

EFRAIM C. GALARRAGA, M.D.

1916-1979

Dr. Efraim C. Galarraga, 63, of Augusta, Maine, died on April 16, 1979 at his home following a brief illness.

He was born in Havana, Cuba on March 29, 1916, the son of Francisco and Rufina Galarraga.

Dr. Galarraga was graduated from the University of Havana, received his medical degree from Havana University Medical School in 1946, and interned and served a residency at the Harlem Hospital in New York City.

He practiced in Roanoke, Virginia and Springfield, Massachusetts until 1965, when he located in Augusta. His hospital appointments include the Burrell Memorial Hospital in Roanoke, the Municipal Hospital in Springfield and the Augusta State Hospital.

Dr. Galarraga was a member of the Kennebec County Medical Association and the Maine Medical Association. He was also a member of the staff at the Augusta General Hospital.

Surviving are his widow, Joyce L. Galarraga of Augusta; four sons, John and Todd of Portland and Danny and Charles of Augusta; and a daughter, Ruth of Augusta.

NAJIB M. PANDYA, M.D.

1928-1979

Dr. Najib M. Pandya, 50, of Lewiston, Maine, died on April 28, 1979 at the Central Maine Medical Center in Lewiston following a long illness.

Born in Bombay, India on July 7, 1928, he was the son of Atmaram and Radhaben Pandya.

He was graduated from N.M. Institute of Science Bombay University and received his medical degree from Grant Medical College Bombay University in 1955. Dr. Pandya interned at the Aultman Hospital in Canton, Ohio and served a residency at the Herman Kiefer Hospital in Detroit, Michigan. His postgraduate courses include the Wayne County General Hospital in Eloise, Michigan and McGill University.

Dr. Pandya practiced in Canton, Ohio, Detroit, Michigan, Montreal, Canada, and in 1966 located in Lewiston, where he became the first full-time psychiatrist and medical director of Child and Family Services. He was instrumental in development of this agency into Maine's first comprehensive community mental health center. As the first chief of psychiatry of St. Mary's General Hospital, he developed the hospital's inpatient psychiatric unit.

He was a member of the Androscoggin County Medical Society, the Maine Medical Association, the American Medical Association, the Maine Psychiatric Association, the American Psychiatric Association, and was a member of the staff of St. Mary's General Hospital and an associate member of the staff at Central Maine Medical Center.

Surviving are his widow, the former Lois Lippiatt of Lewiston; three daughters, Mala Pandya, now studying in Bombay, and Sheila and Sonya Pandya, both of Lewiston; two sons, Rijiv, now studying in Bombay and Robin of Lewiston; a sister, Prabhaben Bhatt of Bombay; and three brothers, Prataprai, Kantilal and Gulabrai, all of Bombay.

RUDOLF E. EYERER, M.D.

1917-1979

Dr. Rudolf E. Eyerer, 61, of Bangor, Maine, died on May 19, 1979 at his home after a long illness.

Born in Munich, Germany on December 23, 1917, he was the son of Georg and Berta Eyerer.

Dr. Eyerer was graduated from Friederich-Wilhelms University in Berlin and received his medical degree from Ludwig-Maximilians University in Munich in 1949. He interned at the IRO General and Chronic Hospital and served residencies at the Free Hospital for Women, the Boston Lying-In Hospital and the Salem Hospital in Massachusetts.

He located in Bangor in 1961, where he was a member of the staff of the Eastern Maine Medical Center, and was employed by Dahl-Chase Pathology Associates.

Dr. Eyerer was a member of the Penobscot County Medical Society, the Maine Medical Association and the American Medical Association.

Surviving are his widow, Joan Eyerer; and four children, Rudolf of Bangor, Daphne of Munich, Juliana Greenleaf of Washington, D.C. and George of Bangor.

ROBERT V. LORIMER, M.D.

1911-1979

Dr. Robert V. Lorimer, 67, of Portland, Maine, died on May 23, 1979 at a local hospital after a short illness.

He was born in Hodgdon, Maine on October 12, 1911, the son of Albert W. and Maude C. Lorimer.

Dr. Lorimer was graduated from the University of Maine, received his medical degree from Harvard Medical School in 1938, interned at Boston City Hospital, and served residencies at the Free Hospital for Women and the Boston Lying-In Hospital. During World War II, he served in the U.S. Army Medical Corps as a Major.

In 1946, Dr. Lorimer located in Portland, where he was a member of the staffs of the Maine Medical Center and Mercy Hospital. From 1967 to 1978, he was chief of staff in the obstetrics and gynecology department at the Maine Medical Center.

He was an affiliate member of the Cumberland County Medical Association, the Maine Medical Association and the American Medical Association. Dr. Lorimer was also a member of the Maine Chapter, American College of Surgeons, the New England Chapter, American College of Obstetricians and Gynecologists, a fellow of the American College of Obstetricians and Gynecologists, the American College of Surgeons and an emeritus fellow of the Obstetrical Society of Boston.

His wife, Lily M. Lorimer, died in 1977.

Surviving are three daughters, Miss Judith M. Lorimer of Pepperell, Massachusetts, Mrs. James Reed of Louisiana and Mrs. John Hewel of Deptford, New Jersey; two sons, Robert D. of Portland and Dr. Craig G. of Madison, Wisconsin; and five grandchildren.

WILLIAM H. AUSTIN, M.D.

1929-1979

Dr. William H. Austin, 49, of Yarmouth, Maine, died on May 26, 1979 in an automobile accident in North Yarmouth.

He was born on November 27, 1929 in Louisville, Kentucky, the son of Arthur H. and Dorothy S. Austin.

Dr. Austin was graduated from Bowdoin College, received his medical degree from Cornell University Medical College in 1956, interned at the Maine Medical Center, and served residencies there and at the Memorial Center in New York City. He served in the U.S. Navy Medical Corps as a Lieutenant Commander from 1962 to 1964.

He had been in private practice in Portland and was involved in research in kidney and lung problems. In 1974, he received an American Heart Association grant to study the balance of acidity and alkalinity in red blood cells. Dr. Austin was staff physician at Pineland Hospital and Training Center in Pownal and was on the staff at the Maine Medical Center and Mercy Hospital.

Dr. Austin was an affiliate member of the Cumberland County Medical Association and the Maine Medical Association.

He is survived by his mother of Cape Elizabeth; a son, Mark C., and a daughter, Jane E., both of New Gloucester; two brothers, John C. of Williamsburg, Virginia and Arthur I. of Calabasas, California; and a sister, Mary S. Austin of Santa Cruz, California.

WESLEY N. WASGATT, M.D.

1911-1979

Dr. Wesley N. Wasgatt, 67, of Rockland, Maine, died on May 27, 1979 at a Rockland hospital after a brief illness.

He was born in Rockland, Maine on June 25, 1911, the son of Dr. Rowland J. and M. Josephine Wasgatt.

Dr. Wasgatt was graduated from the University of Maine and received his medical degree from Columbia University College of Physicians and Surgeons in 1937. He interned at the Rhode Island General Hospital and served a residency at the Providence Lying-In Hospital. From 1942 to 1946, he served in the U.S. Army Medical Corps.

In 1946, he located in Rockland where he was affiliated with the Knox County General Hospital and the Camden Community Hospital.

He was a member of the Knox County Medical Society, the Maine Medical Association and the American Medical Association.

Surviving are his widow, Eleanor C. Wasgatt of Rockland; a daughter, Mrs. Kenneth Hoffer of Santa Monica, California; two sons, Rowland, II of Fort Collins, Colorado and Charles of Melrose, Massachusetts; three sisters, Miss Mary Wasgatt of Rockland, Miss Martha Wasgatt of Farmington and Mrs. Cynthia McBride of Laurel Springs, New Jersey; eight grandchildren and a niece.

G. PATRICK SHAW, M.D.

1929-1979

Dr. G. Patrick Shaw, 49, of Saco, Maine, died suddenly on June 24, 1979 in Waterville.

Born in Manistique, Michigan on August 2, 1929, he was the son of Dr. George A. and Isabella C. Shaw.

Dr. Shaw was graduated from Alma College in Michigan and received his medical degree from the University of Maryland School of Medicine in 1957. He interned and served a residency at the Harper Hospital in Detroit, Michigan. From 1959 to 1961, he served in the U.S. Navy as a Lieutenant.

In 1961, he located in Saco. He was chief of obstetrics and gynecology at Webber Hospital in Biddeford and Vice President of the hospital medical staff.

Dr. Shaw was a member of the York County Medical Society, the Maine Medical Association and the Maine Society of Obstetrics and Gynecology.

He is survived by his mother; his widow, Elizabeth S. Shaw; a son, George Jeffrey, and a daughter, Victoria Margaret, all of Saco; and a brother, Dr. T. Michael Shaw of Travers City, Michigan.

CHARLES P. CLARKIN, M.D.

1910-1979

Dr. Charles P. Clarkin, 68, of Portland, Maine, died at a local hospital on July 13, 1979 after a long illness.

Born in Providence, Rhode Island on September 8, 1910, he was the son of Arthur J. and Mary U. Clarkin.

He was graduated from Providence College, received his medical degree from Georgetown University School of Medicine in 1937, interned at the Bridgeport Hospital in Connecticut, and served a residency at the Rhode Island Hospital.

During World War II, he served in the U.S. Army Air Force as surgeon in the Pacific. He retired with the rank of Colonel.

In 1949, he came to Portland and served as radiologist at Mercy Hospital. He later was appointed chief of radiology at the Notre Dame and Webber Hospitals in Biddeford with which he was associated for 23 years. He retired in 1973.

Dr. Clarkin was an affiliate member of the Cumberland County Medical Association, the Maine Medical Association, the American Medical Association, the American Board of Radiology and the Maine Radiological Society.

Surviving are his widow, Mary E. Clarkin; three daughters, Mrs. Charles E. Poor of Whitman, Massachusetts, Mrs. Dwight M. Bonk of Buffalo, New York and Miss Gale F. Clarkin of Portland; a son, Stephen C. Clarkin of Portland and Augusta; two sisters, Mrs. James P. Gallogly of Matunuck, Rhode Island and Mrs. Donald P. Gamble of Wilmington, Delaware; a brother, Dr. Arthur J. Clarkin of East Greenwich, Rhode Island; and four grandchildren.

WILLIAM SPEAR, M.D.

1909-1979

Dr. William Spear, 69, of West Bowdoin, Maine, died at his home on September 25, 1979 after a long illness.

Born in Boston, Massachusetts on October 9, 1909, he was the son of Louis and Anna Spear.

He was graduated from Bates College, received his medical degree from Boston University Medical School in 1941, and interned at the Central Maine Medical Center in Lewiston. During World War II, he served in the U.S. Air Force as a Major.

Dr. Spear had practiced in Lisbon Falls for 30 years, retiring in 1976. He was Lisbon's health officer for several years. Dr. Spear organized and helped found the Central Maine Medical Center's emergency room, where he also served as chief of emergency room services.

He was an affiliate member and past president of the Androscoggin County Medical Society, a member of the Maine Medical Association, the American College of Emergency Physicians, and charter member and first president of the Maine Chapter of the American College of Emergency Physicians.

Surviving are his widow, Marion Spear of West Bowdoin; two sons, Robert L. Spear of Lee, Massachusetts and Stephen B. Spear of Brooklyn, Connecticut; a daughter, Kathryn Spear of Kittery; a brother, Oscar Spear of Bridgeport, Connecticut; a sister, Sophia Kaufman of Cambridge, Massachusetts; and three grandchildren.

WILLIAM O. BUELL, M.D.

1918-1979

Dr. William O. Buell, 60, of Saco, Maine, died unexpectedly at

a York hospital on September 15, 1979.

He was born in New York City on December 14, 1918, the son of Dr. Kenneth W. and Katherine M. Buell.

Dr. Buell was graduated from Columbia College and received his medical degree from Columbia University College of Physicians and Surgeons in 1943. He interned at the Bellevue Hospital in New York, served residencies there and at the Lenox Hill Hospital in New York, and was on the staff in the woman's division at St. Luke's Hospital and Polyclinic Hospital.

During World War II, he was a Captain in the U.S. Army Medical Corps.

In 1968, he began a private practice in obstetrics and gynecology in Biddeford. Dr. Buell was on the staff at Webber and Mercy hospitals.

Dr. Buell was an affiliate member of the York County Medical Society, the Maine Medical Association and the American Medical Association. He was also a fellow of the American College of Surgeons and a member of the American College of Obstetrics and Gynecology.

Surviving are his widow, Anne M. MacDonagh of Saco; two sons, William, Jr. and Thomas, both of Saco; two daughters, Kathryn Harlow of Kennebunkport and Ann Baum of Katonak, New York; and two grandchildren.

WILLIAM A. PURINTON, M.D.

1905-1979

Dr. William A. Purinton, 74, of Goulds Landing, Pushaw Lake, husband of the late Evelyn T. Purinton, died on October 2, 1979 at his home.

He was born in Kenduskeag, Maine on February 17, 1905, the son of Dr. Watson S. and Nellie M. Purinton.

Dr. Purinton was graduated from the University of Maine and received his medical degree from Tufts University School of Medicine in 1933. He interned at the Pawtucket Memorial Hospital in Rhode Island and served residencies at the Charles V. Chapin Hospital in Providence, Rhode Island and Eastern Maine General Hospital in Bangor.

He had practiced in Bangor since 1936, and was a surgeon at the Bath Iron Works during World War II. Dr. Purinton was a staff member of the Eastern Maine Medical Center and St. Joseph Hospital, and was the organizer of the out-patient department of St. Joseph Hospital and director of the ward.

Dr. Purinton was a senior member of the Penobscot County Medical Society and the Maine Medical Association. He was also a member of the American College of Emergency Physicians.

Surviving are three daughters, Mrs. James Shanaberger of Wurtsmith AFB, Michigan, Mrs. John Suggs of New Cumberland, Pennsylvania and Mrs. Dean Beaulieu of Old Town; one brother, Earle W. Purinton of Falmouth Foreside; two sisters, Mrs. Alvin Giffin of Fort Meyers, Florida and Mrs. Bernice P. Webster of Boise, Idaho; seven grandchildren and several nieces and nephews.

ASA C. ADAMS, M.D.

1899-1979

Dr. Asa C. Adams, 80, of Orono, Maine, former President of the Maine Medical Association from 1968-1969, died unexpectedly on October 2, 1979 at his home.

Born in Linneus, Maine on May 18, 1899, he was the son of George H. and Phoebe Adams.

Dr. Adams was graduated from Colby College and received his medical degree from the University of Vermont College of Medicine in 1928. He interned at the Eastern Maine General Hospital and took postgraduate courses at the Massachusetts Medical Center and Lahey Clinic. He served in the U.S. Army during World War I, and was a 1st Lieutenant in the U.S. Army Medical Reserves from 1928 to 1934.

In 1929, he established a practice in family medicine and general surgery in Orono. Following 43 years of practice, he retired in 1972. Dr. Adams was a member of the staff and former chief of surgery at Eastern Maine Medical Center, and a member of the

staff at St. Joseph Hospital.

An honorary member of the Penobscot County Medical Society and the Maine Medical Association, he received a 50-year pin in 1978. He was also a member of the American Medical Association. Dr. Adams was President-elect of the M.M.A. from 1967-1968, Council Chairman in 1966-1967 and, prior to that, had served as Councilor for the First District. He also served as a Delegate and Alternate Delegate to the American Medical Association.

His wife, Vina P. Adams, died in April of 1978.

Surviving are two sons, Dr. Marvin C. Adams of Cape Elizabeth and Dr. David L. Adams of Cumberland Foreside; eight grandchildren and two great-grandchildren.

HARRY A. NAUMER, M.D.

1894-1979

Dr. Harry A. Naumer, 85, of Port Clyde, Maine, died at a Rockland convalescent home on October 6, 1979.

Born in New York City on July 23, 1894, he was the son of Charles and Anna H. Naumer.

Dr. Naumer was graduated from Columbia College and received his medical degree from Columbia University College of Physicians and Surgeons in 1918. He interned at the Brooklyn Hospital, served a residency at the Babies Hospital in New York City from 1919 to 1920, and did postgraduate work at the Children's Hospital in Boston.

Specializing in pediatrics, his hospital appointments in New York included the Greenpoint, Brooklyn and Long Island College hospitals. In the 1950's, he located in Port Clyde where he was affiliated with the St. George Child Health Clinic until 1968, and was a consulting pediatrician at the Knox County General Hospital.

An honorary member of the Knox County Medical Society and the Maine Medical Association, he received a 50-year pin in 1968, a 55-year pin in 1973 and a 60-year pin in 1978. He was also a member of the American Medical Association and the American Board of Pediatrics.

Surviving are his widow, Elizabeth H. Naumer of Port Clyde; two daughters, Mrs. David Brown of Darien, Connecticut and Mrs. William Dennen of Thomaston; six grandchildren and two great-grandchildren.

EUGENE B. GRIFFITHS, M.D.

1904-1979

Dr. Eugene B. Griffiths, 75, of Presque Isle, Maine, died at his home on November 1, 1979 following a long illness.

He was born in Woodstock, N.B., Canada on July 8, 1904, the son of Benjamin and Mary Griffiths.

Dr. Griffiths was graduated from the University of Maine, received his medical degree from McGill University Faculty of Medicine in 1931 and interned at the Montreal General Hospital.

He located in Presque Isle in 1932, and was affiliated with the Arthur R. Gould Memorial Hospital. Dr. Griffiths retired in 1975.

Dr. Griffiths was a senior member of the Aroostook County Medical Society and the Maine Medical Association.

Surviving are his widow, Kathryn P. Griffiths of Presque Isle; two sons, David Griffiths and Stephen Griffiths, both of Presque Isle; one daughter, Mrs. Andrew J. Ives of Santa Fe, New Mexico; and ten grandchildren.

CHARLES F. BRANCH, M.D.

1897-1979

Dr. Charles F. Branch, 82, of Auburn, Maine, Maine's first Chief Medical Examiner and former President of the Maine Medical Association from 1969-1970, died on November 14, 1979 at his home following a long illness.

Born in Amherst, Massachusetts on August 14, 1897, he was the son of Dr. Charles F. and Clara G. Branch.

Dr. Branch was graduated from St. Johnsbur Academy in Vermont, received his medical degree from the University of Vermont

College of Medicine in 1923 and served a residency in pathology at the Boston City Hospital. Dr. Branch taught at Jefferson Medical College in Philadelphia from 1925 to 1926 and at Boston University from 1926 to 1946. He was professor of pathology at Boston University from 1932 to 1946, dean of the medical school from 1943 to 1946 and was associate director of Evans Memorial for Clinical Research from 1939 to 1944.

He was licensed as a specialist by the American Board of Pathologists in 1937. From 1946 to 1947, he was executive director of the Children's Medical Center in Boston and from 1947 to 1950, assistant director of the American College of Surgeons.

In 1950, Dr. Branch was appointed director of Laboratories and Pathologist-in-Chief at the Central Maine General Hospital in Lewiston. He had served as consulting pathologist at the Rumford Hospital, Franklin County Memorial Hospital, Goodall Hospital and Stephens Memorial Hospital and as medical examiner for Androscoggin County. He was also one of the founders of the Maine

Pathological Society and the Maine Medico-Legal Society, of which he was president from 1961 to 1963.

Dr. Branch was appointed Maine's first Chief Medical Examiner in May 1968. This position was created by the legislature in special session in January 1968 to give the State some central direction and supervision in the medical-legal aspects of homicides and unattended or unexplained deaths.

An honorary member of the Androscoggin County Medical Society and the Maine Medical Association, he received a 50-year pin in 1973 and a 55-year pin in 1978. Dr. Branch was President-elect of the M.M.A. from 1968-1969, Council Chairman in 1967-1968 and, prior to that, had served as Councilor for the Second District. He was also a member of the American Medical Association.

Surviving are his widow, the former Mary Chapman; two sons, Nicholas of Portland and Christopher of Auburn; and a daughter, Betty Ann of New York City.

News, Notes & Announcements

Dr. Brownlow Joins Augusta

Naval Reserve Medical Contingency Response Unit 101

Dr. Bradley Brownlow, of Blue Hill, a Captain in the Medical Corps, United States Naval Reserve, has affiliated with MED CRU 101, drilling at Augusta. Dr. Brownlow whose specialty is Family Practice, previously served at CO of Surgical Team 201, in Portland.

The Augusta Reserve Center needs physicians who hold Reserve Commissions. Drills are held the first weekend of each month and pay billets are available. Interested Doctors should contact LCDR James J. Quinn at 622-6171, extension 230.

Southern Maine—Emergency Physician—St. Mary's General Hospital is seeking a career emergency physician for a full time opening beginning approximately January 1, 1980. A physician seeking active involvement with administration, fellow emergency physicians, and medical staff, to assist in the development of the new and exciting specialty of emergency medicine, will be selected. St. Mary's is an active 240 bed acute care community hospital with an active role in telemetry/medical control of prehospital activities. Salary and fringe excellent. Unparalleled 4 season and ocean recreational opportunities. Reply in confidence to David Eitel, M.D., E.M.S. Office, 45 Golder Street, Lewiston, Maine 04240 or call (207) 786-2901, extension 369.

CONTINUING MEDICAL EDUCATION IN MAINE—Continued from Page 24

Category I and AAFP (elective). These programs may be viewed over ITS. For further information contact David R. Ginder, M.D.; 873-0621.

Sebasticook Valley Hospital Pittsfield, Maine

Feb. 6, 1980 **Blood Gases**
9:30 a.m.-12 N Richard Dole, M.D., Sebasticook Valley Hospital
This program has been certified AMA Category I and AAFP (elective).
For further information contact David R. Ginder, M.D.; 873-0621.

V. A. Hospital Togus, Maine

Jan. 21, 1980 **General Staff Meetings**
2 p.m. Speaker and subject to be announced
2nd Tues. ITS presentation
12 Noon

Medical Service Staff Meetings

Every Wed. Staff Meeting
1:15 p.m.
2nd Wed. Review of Records
1:15 p.m.
Every other Oncology Clinic
Thurs.

Feb. 15, 1980 **Neurology Lecture**
11 a.m. Stephen Dell, M.D., Chief of Neurosurgery, Boston VA Hospital

These programs have been certified AMA Category I. For further information contact E. Osborne Coates, Jr., M.D.; 623-8411.

ANNOUNCEMENT: Medical Care Development, Inc. is now receiving a listing of continuing medical education activities taking place in Vermont, New Hampshire, and Massachusetts. If you wish further information about these programs, please call Gerald Goold; 622-7566.

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Letters to The Editor

To The Editor:

I commend Dr. Katz on his article, "Pragmatic Approach to Carcinoma of the Lung", Vol. 70, No. 7, July 1979. Unfortunately he has overlooked an extremely valuable diagnostic tool.

Computed tomography has the unique ability to present a three dimensional image of the thorax free of confusing overlapping structures allowing for an accurate analysis of the extent and location of disease. When combined with 22 gauge "skinny" needle aspiration complete diagnosis and staging can be performed as an outpatient procedure, quickly, safely, accurately and at much less expense, and morbidity than the traditional bronchoscopy, mediastinoscopy, thoracotomy sequence. This technique has permitted only potentially curable patients to undergo surgery while developing logical alternative modes of therapy for those with metastatic fungal, opportunistic or other lesions in the chest, not requiring an operation.

BARRY KUTZEN, M.D.
Department of Radiology
Central Maine Medical Center
Lewiston, Maine 04240

To The Editor:

Re: Cimetidine Treatment of Pruritus in Polycythemia Vera

Pruritus, a common symptom in polycythemia vera, appears histamine mediated.¹ It can be troublesome despite therapy but may be relieved with chemotherapy. Recently a letter in the *New England Journal of Medicine* reported dramatic resolution of severe and intractable pruritus with a histamine H₂ receptor antagonist, cimetidine. The following case is presented to further illustrate the potential usefulness of cimetidine.

A 78-year-old man presented with polycythemia vera in July 1976. Pruritus and recurrent phlebitis were the predominant symptoms. He was treated with phlebotomies and chlorambucil (6 mg/m² daily). A complete remission was obtained and his symptoms completely disappeared. Chlorambucil was discontinued in December 1978. He was symptom-free until August 1979, when he redeveloped severe pruritus, especially after bathing. At that time, despite normal peripheral blood counts, bone marrow examination revealed striking hypercellularity with panmyelosis. Two-week trials of diphenhydramine, hydroxyzine, and cyproheptadine were unsuccessful in relieving his symptoms. Cimetidine 300 mg, four times daily was initiated. Within five days there was complete resolution of his pruritus; post-bathing symptoms were reduced to 10% of his original pre-treatment level.

Although the pruritus in polycythemia vera is thought to be histamine H₁ receptor mediated,¹ the patient in the first report² and the patient presented here responded to a histamine H₂ receptor antagonist. This mode of therapy may have important implications in the management of polycythemia vera as an adjunctive measure along with other therapy, or as symptomatic measure when other therapy may not be necessary or indicated.

REFERENCES

1. Gilbert, H.S., Warner, R.P., Wasserman, L.R.: A study of histamine in myeloproliferative disease. *Blood* 28:795, 1966.
2. Easton, P., Galbraith, P.R.: Cimetidine treatment of pruritus in polycythemia vera. *N Eng J Med* 299: 1134, 1978.

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County Society Notes

Somerset

The regular meeting of the Somerset County Medical Society was held at the Whittemore Restaurant in Skowhegan on April 18, 1979.

There were 14 members present and Dr. Francis I. Kittredge, President of the Maine Medical Association.

The minutes of the last meeting were read, and accepted as read.

Dr. Kittredge was introduced to the members by Dr. Steeves. The President of the M.M.A. re-emphasized the need of a new building for the headquarters of the organization in Augusta because of the termination of our space in Brunswick. The different optional plans were discussed at length, and the cost of each plan with the different assessed value to each member.

Dr. John Steeves made another motion to the floor that the Delegates go back and rescind the plan C that the Delegates of the House voted in of the last meeting held in April 1979 in Waterville. This was seconded by Dr. Robert Steinhacker. Dr. Steeve's motion was defeated by vote in the floor.

Finally, it was decided that Dr. Lester Henderson will pass to each member of the different optional plans, A, B, C and D and will let each member vote on it. Seventeen members returned the hand-out of the four different option plans. Three members voted for option plan A; and fourteen voted for option plan C.

The meeting was adjourned at 9:00 p.m.

VINCENTE L. SY, M.D., *Secretary*

York

The May meeting of the York County Medical Society was held on May 9, 1979 at the Webber Hospital in Biddeford.

The program was as follows: social hour, 6:30-7:30 p.m.; dinner, speaker and business meeting to follow.

The speaker was Michael Petit, Commissioner, Maine Department of Human Services, Bureau of Health, State House, Augusta. His subject was "Matters Concerning the Maine Department of Human Services and Issues on Health." Mr. Petit gave a very comprehensive and detailed discussion concerning the above subject. This talk was replete with questions and answers.

Following this talk, the business meeting was called to order by our President, Dr. Connor Moore.

The minutes of the last meeting were dispensed in the interest of time, because of the length of the talk and the hour.

There was no old or new business.

The following announcements were made:

1. The October meeting of the York County Medical Society will be held in York, Wednesday, October 10, 1979. Place of meeting to be announced. Committee in charge: Drs. Kenneth Leigh, Mirle Kellett, and Alvin Hoffman.

2. Annual Meeting of the Maine Medical Association to be held at the Treadway-Samoset, Rockport, Maine, June 16-19, 1979.

The report of the meeting of the House of Delegates held at the Mid-Maine Medical Center in Waterville, April 7, 1979 was given by Dr. Carl Richards.

Again due to the lateness of the hour, there was very little business conducted.

There were 20 physicians and guests present; another disappointing turnout.

The meeting was there upon adjourned.

MELVIN BACON, M.D., *Secretary*

Penobscot

The May meeting of the Penobscot County Medical Society was held at the Penobscot Valley Country Club in Orono on May 15, 1979. About 45 members attended. The meeting was opened by Dr. David Beebe, after which the previous minutes were approved without addition or change.

The free second surgical opinion program was once again discussed at great length. A motion was made by Dr. Richard Gaillard to send out a questionnaire and implement the program if surgeons receiving the questionnaire were in favor of it. This motion was seconded and carried by a 34 to 10 vote.

Dr. Beebe then called upon the resolutions committee and Dr. Frederick Emery presented a resolution on the passing of Dr. Donald Coulton, which shall become a permanent part of the records of the Penobscot County Medical Society and a copy of which shall be sent to Dr. Coulton's widow.

Dr. Rudolf Eyerer was then elected to affiliate status by unanimous vote. Two new applications for membership were presented to the Society; that of Drs. Edward M. Sipple, a radiologist practicing in Millinocket and Robert W. Haerberlein, Jr., a dermatologist who plans to practice in Bangor. Both of these candidates were elected to membership by written ballot.

Following this, Dr. Lightbody summarized Executive Committee proceedings for us and mentioned plans for collecting contributions to provide retiring Executive Director Dan Hanley with an appropriate gift. This was discussed at some length and was voted unanimously that a gift be appropriated from the treasury of the Penobscot County Medical Society and sent to Patricia Bergeron to be used as a portion of a retirement gift for Dr. Hanley. Dr. Michael Solomon, the treasurer, was instructed to send the money as directed.

Dr. H. Clement Jurgeleit then presented the new slate of officers for the coming year. The nominating committee elected the following officers:

President: Dr. Robert P. Andrews, Bangor
President Elect: Dr. Sidney R. Block, Bangor
Treasurer: Dr. Michael B. Bruehl, Orono
Secretary: Dr. James R. Curtis, Bangor

Counselors and members of the Executive Committee: Drs.

William E. Clark, Jr., Francis I. Kittredge and Thomas L. Watt, all of Bangor

The secretary was instructed by the membership to cast one ballot approving the choice of the nominating committee and this was done. Dr. Jurgeleit then read a list of the Delegates and Alternate Delegates from our Society. The following are Delegates: Drs. H. Clement Jurgeleit, Jack N. Meltzer, Robert D. Tomlinson, Thomas Watt, Denis F.J. Halmagyi, R. Russell Lang, James R. Curtis, all of Bangor and A. Dewey Richards, Orono. The Alternate Delegates: Drs. William E. Clark, Jr., Don L. Maunz, Leonard J. Levy, G. Vernon A. MacDonald, Patrick W. Kamm, John S. Kaiser and Donald W. Krause, all of Bangor.

The Delegates were then instructed by the membership concerning the resolutions which shall be presented at the June meeting of the House of Delegates. It was felt that Executive Committee resolution No. 3 should be supported by our Delegates. Executive Committee resolution No. 4 should be assessed on its merits when reported out of reference committee. Penobscot County resolution, although not applicable at present, was felt to still be pertinent in that the intent of fairly assessing the users of the building should be supported. Finally, it was felt by the Penobscot County membership that the York County motion could not be supported as written.

Following this rather full schedule of business, Dr. David Beebe and the officers for 1978 and 1979 were thanked and congratulated for the work they had done on behalf of the members of the County Medical Society.

There being no further business, the meeting was adjourned by Dr. David Beebe sometime after 9:30 p.m.

JAMES R. CURTIS, M.D., *Secretary*

Aroostook

The annual meeting of the Aroostook County Medical Society was held at the Northeastland Hotel in Presque Isle on June 13, 1979.

The scheduled meeting of the Society in May was not held due to lack of a quorum.

The meeting was called to order by the President, Dr. Arthur K. Carton, with 19 members in attendance.

The minutes of the previous meeting were read and accepted. The secretary also reported that a majority of the membership had returned the voting cards on the revised Bylaws and that these were unanimously in favor of the revision.

Dr. Craig W. Young expanded on his request for reimbursement of expenses incurred attending an advanced Seminar on Physician Negotiations held in Danvers, Massachusetts which was mentioned in the minutes of the previous meeting and reported on matters covered at this Seminar. Dr. Young stated that contracts negotiated with a hospital may be regarded as price fixing by the Federal Trade Commission. The A.M.A. will review any such contracts on request and give an opinion. It was moved, seconded, and voted that Dr. Young be reimbursed in full for his expenses.

The establishment of a clinic in Madawaska was discussed and it was voted not to object to a clinic in that area.

The matter of a retirement gift for Dr. Dan Hanley was discussed and it was voted to refer this matter to the Maine Medical Association for appropriate action.

The applications of Drs. Kenneth D'Amato of Eagle Lake and Thomas Booth of St. Francis, osteopathic physicians for membership in the Society, were presented. After some discussion, these applications were approved and they were elected to membership.

A nominating committee consisting of Drs. Aungst, Pendleton and Giberson was appointed by the president. They presented the following slate of officers:

President: Dr. Rodrigue J. Albert, Fort Kent

Vice President: Dr. Laurence A. Watterson, Presque Isle

Secretary: Dr. Janet M. Parker, Houlton

Treasurer: Dr. Samuel Rideout, Fort Fairfield

Delegate to the M.M.A. House of Delegates: Dr. Alroy A. Chow, Presque Isle (3 yrs.)

Alternate Delegate: Dr. Che To Ho, Caribou (3 yrs.)

No nominations appearing from the floor, the above slate was unanimously elected. The nominating committee also suggested the names of Drs. Melvin Aungst and Craig Young as candidates for the Executive Committee of the Maine Medical Association. Both of these names were approved by the Society.

Dr. Young gave a report on the meeting of the Health Care Financing Committee of which he is a member. Special reference was made to the Medicaid fee schedule and to relative value scales. The possibility of a new Blue Shield fee schedule was also discussed. Motion was made to instruct our delegates to support the concept of equal reimbursement to participating and non-participating physicians by Blue Shield. This motion was seconded and passed.

The report of the treasurer was read, accepted, and placed on file.

Dr. Alroy Chow reported on the ad hoc committee for long-range planning of the area hospitals. He suggested that each of us investigate the progress made by our local hospital planning committee with reference to the selection of a hospital planner for the area. This provoked some discussion of the defects of the planning concept and whether the Society should or should not seek to have any input in long-range planning. No decision was reached and no motion was made.

Dr. Donald Brushett commented briefly on a recent meeting with the Aroostook County Action Program in regard to their establishment of a clinic in the Houlton area despite the opposition of the local physicians. This matter will be discussed in greater detail at a subsequent meeting.

No further business appearing, the meeting was adjourned.

GEORGE J. HARRISON, M.D., *Secretary*

Knox

The Knox County Medical Society met at the Sail Loft Restaurant in Rockport on September 11, 1979.

Thirty members were in attendance. Mr. William Bradley, a medical student in the area, was an invited guest and Mr. Frank O. Stred was an invited guest.

Following dinner, Mr. Frank Stred, Executive Director of the M.M.A., addressed the Society regarding the current and future problems for the M.M.A. Topics of interest were the current fiscal position of the M.M.A., the legislative lobbying efforts of the M.M.A., the ongoing negotiations with Blue Shield, and the relationship of our Society to other health care providers. Mr. Stred commented widely on the role of the M.M.A. and these issues, and the effort made by the M.M.A. to serve its membership.

There being no further business, the meeting was adjourned at 9:30 p.m.

The Knox County Medical Society met at the Sail Loft Restaurant in Rockport on October 2, 1979.

Twenty members were in attendance. Invited guest was Dr. Henry Hardy.

Following dinner, a short business meeting was called to order and Dr. John Cox was voted unanimously into membership. The membership of Dr. Michael James was tabled due to the fact that no one present had any firsthand knowledge of him. The secretary was directed to indicate this action to Dr. James and invite him to make himself known to the members of the Knox County Medical Society. The president also indicated that she will appoint a nominating committee for officers within the next month; such a committee to nominate a replacement for Dr. Wickenden who is a member of the M.M.A. Executive Committee whose term expires next year. The secretary indicated to members present that anyone wishing to serve on any of the standing and/or special committees of the Maine Medical Association should make that wish known to the nominating committee.

Following the business meeting, Lewis Pelletier, Ph.D., audiologist and director of the Mid-Coast Speech and Hearing Center, presented a discussion of impedance, audiometry, and middle ear dysfunction. In addition, he emphasized the need for earlier and more complete screening of children for hearing loss.

There being no further business, the meeting adjourned at 9:30 p.m.

ALBERT J. LANTINEN, JR., M.D., *Secretary*

Lincoln-Sagadahoc

The regular meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges in Wiscasset on September 18, 1979, with thirty-five members and guests present.

The May minutes were accepted as read by the secretary. Dr. Gerry Hayes discussed the June meeting of the M.M.A. House of Delegates.

The Board of Censors presented three names in nomination for active membership, and those present unanimously approved the applications of Drs. Gregory A. Kelly, Bath, Everett D. Schubert, Damariscotta and John C. Skillings, Brunswick.

Dr. Robert McAfee, of Portland, spoke on the AMA and major actions of its recent meeting of the House of Delegates.

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held at the Ledges in Wiscasset on October 16, 1979.

There were twenty-five members and guests present. The meeting was opened by President Cote; the minutes of the September meeting were read by the secretary and approved as read.

The treasurer recommended that the 1980 dues be set at \$55.00; the motion was made and passed.

Dr. Elihu York requested transfer to service membership, and the members so voted.

A letter from M.M.A. was read requesting nomination of a member to represent the Society on the M.M.A. Executive Committee for the first six months of 1980. The Society voted that, since the nominating committee has not yet met, and there is county representation among the officers currently on the Executive Committee, no name be forwarded at this time.

Dr. Cote appointed Drs. Avantaggio, Burden and Schall to serve on a nominating committee to bring in a slate of officers for the December meeting.

Dr. Schmidt then presented a movie on Upper Gastrointestinal Endoscopy, with comments by Drs. Kelly and Skillings.

GEORGE W. BOSTWICK, M.D., *Secretary*

Oxford

The October meeting of the Oxford County Medical Society was held on October 10, 1979 at The Bethel Inn in Bethel. Ten active members, one senior member and one member-elect were present. Dr. Brinton T. Darlington, President of the Maine Medical Association, was also in attendance.

The meeting was called to order by Dr. H. Richard Bean, President.

Guest speaker, Attorney Guy P. Seaberg, Chief, Medicaid Fraud Control Unit of the Department of the Attorney General, explained the function of his new department and requested cooperation from the Society members. Dr. Darlington pointed out that the American Medical Association supports this program.

Dr. Darlington informed the Society that the Maine Medical Association decided not to build a new building. An older building was acquired and the offices have been moved to this building at 524 Western Avenue in Augusta. Negotiations with Blue Cross are still progressing. It was suggested that the Society should not entertain any discussion which violates the antitrust laws.

A communication from Dr. Melvin Bacon, Chairman of the Diabetes Committee, was read. It was unanimously decided that both Rumford Community and Stephens Memorial undertake public education programs during the month of November.

A letter from Mr. Frank O. Stred, Executive Director of the Maine Medical Association, was brought before the Society. It was decided to invite Mr. Stred to our January meeting.

The Committee on Nominations recommended the following slate of officers for 1979-1980, and nominations were unanimously accepted:

President: Dr. Linwood M. Rowe, Rumford
 Vice President: Dr. Robert B. Funch, Norway
 Secretary-Treasurer: Dr. Usha Wadhwa, Dixfield
 M.M.A. Executive Committee Representative: Dr. David L. Phillips, Rumford

The treasurer's statement was read and approved.

Scheduling of Society meetings to be held in January, March and May 1980 was undertaken. The next Society meeting will be held on Wednesday, January 9 and is tentatively scheduled for The Bethel Inn.

There being no further business, the meeting was adjourned, following which dinner was enjoyed by all.

HARBANS S. SODHI, M.D., *Secretary*

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Contraindications: Patients with known hypersensitivity to the drug

Warnings: Warn patients that mental and/or physical abilities required for tasks such as driving or operating machinery may be impaired, as may be mental alertness in children, and that concomitant use with alcohol or CNS depressants may have an additive effect. Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression, suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction, changes in EEG patterns (low-voltage fast activity) may appear during and after treatment, blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Usual Daily Dosage: Individualize for maximum beneficial effects. *Oral-Adults:* Mild and moderate anxiety and tension, 5 or 10 mg *t.i.d.* or *q.i.d.*; severe states, 20 or 25 mg *t.i.d.* or *q.i.d.*. *Geriatric patients:* 5 mg *b.i.d.* to *q.i.d.* (See Precautions.)

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County Society Notes

Penobscot

The first meeting of the 1979-1980 season of the Penobscot County Medical Society was held on September 18, 1979, at Pilots Grill in Bangor. Forty-eight members attended and there were two guests, our featured speaker, Executive Director of the Maine Medical Association, Mr. Frank O. Stred, and Dr. Rick Mazzei, an Orthopedic Surgeon locating in Bangor.

The meeting was opened by Dr. Robert P. Andrews and the May 1979 minutes were approved as published without addition or change. Dr. Andrews then outlined the planned format for the year. It was decided to meet regularly at Pilots Grill the third Tuesday of each month with dinner being served at 7:00 p.m. The decision to concentrate on Society and State medical business, rather than education and technical subjects was reaffirmed for this year.

Dr. Robert Haeberlein, Jr., a dermatologist who has recently arrived, was introduced to the membership by Dr. Andrews. Following this, Dr. Thaddeus Jozefowicz was nominated to fill the post of County Medical Society Treasurer vacated by Dr. Michael Bruehl. Dr. Jozefowicz was elected to the post by written ballot.

Several applications for membership to the Society were considered. There were seven applications for junior membership submitted by resident physicians in the Family Practice program at Eastern Maine Medical Center. The names of the residents are as follows: Drs. Diane Korsower, Curtis Smith, David Axelman, Robert Baroody, Mary L. Barnhart, Richard Sagall and Diana Jeannotte. All of the residents mentioned were elected to junior membership by written ballot.

In addition to the junior members, five physicians applied for active membership. Their names are as follows: Drs. Rowland Pritchard, John Schroder, Donald Clough, Won Chung and Eric Miller. All five of the applicants were elected to active membership by written ballot.

Dr. Francis I. Kittredge then introduced the Executive Director of the Maine Medical Association, Mr. Frank O. Stred, who spoke about the various issues concerning the Association and County Society at this time. He touched on problems involving finances, changing relationships with insurance carriers and anticipated political and legislative activity. Following his talk, there was a very lively question and answer period which indicated interest and concern regarding the future of medical practice in our State.

Dr. Andrews then made a few additional comments, primarily concerning legislative matters and the need for greater awareness on the part of the practicing physician of the changing structure of medical practice.

There being no further business, the meeting was adjourned at about 9:30 p.m.

The October meeting of the Penobscot County Medical Society was held on October 16, 1979, at Pilots Grill in Bangor. Forty-six members were present and one guest, Mr. Guy P. Seaberg.

The meeting was opened by Dr. Andrews and the minutes of the September meeting were approved after a minor change. The change involved Dr. Eric Miller. He was erroneously placed in the category of junior member. Dr. Miller was elected to active membership in the Penobscot County Medical Society.

Applications of Drs. Richard Schwartz and Richard Mazzei were presented to the membership by Dr. Andrews, as was an application for junior membership by Dr. Michael Klein. These three applicants were elected to membership by written ballot.

Dr. Patrick Kamm of Bangor was appointed as representative to the Executive Committee of the Maine Medical Association. Dr. Leonard Levy was appointed to the position of Delegate to the Maine Medical Association to replace Dr. Donald Krause.

Dr. Andrews reported on the finding of Dr. Beebe's survey concerning a free second opinion program for Penobscot County. Apparently, the survey indicated an approximately equal split between those in favor and those opposed to the free second opinion program. It was therefore felt that under these circumstances it would not be reasonable to proceed with the program.

Mr. Guy P. Seaberg, Assistant Attorney General and Chief of

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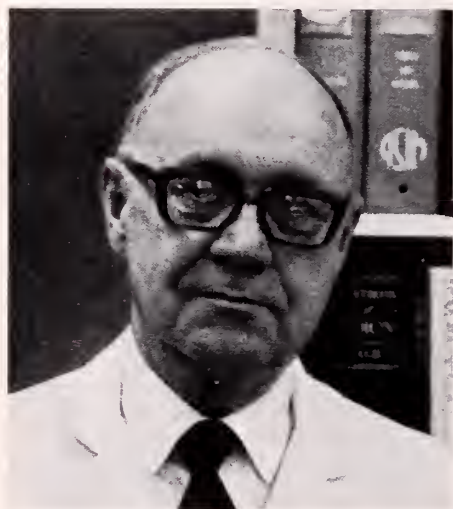
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*PATIENT CARE Magazine—Outlook 1977, "Face-Off: Cost Containment vs. Chaos," January 1, 1977.

Lyle CB, et al. "Practice habits in a group of eight internists," ANNALS OF INTERNAL MEDICINE 84 (May 1976), 594-601.

Schroeder SA, et al. "Use of laboratory tests and pharmaceuticals: variation among physicians and effect of cost audit on subsequent use," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 225 (Aug. 20, 1973), 969-73.



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The Journal of the Maine Medical Association

Volume Seventy-one

Augusta, Maine, February, 1980

Number 2

Anorexia Nervosa

Kafka's artist pales at your greedy fast.
Sitting bulge-eyed he absorbs beauty's invisceration on
lattices softened by tears drawn taut across scaphoid
cheeks.

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while perched at extinction's edge.
Boned and skinned by yesterday's hates, choosing
holocaust's camps, easily ignoring minions of festive
treats.

Soothsaying analysts, seekers, planners, pardon the
prison, forgive the pangs of your marasmus.
Unknowing they see doll-like clothes which surround
the egg shell skin. Inside stuffed and wasted you
crouch in rage, and unless soon sated—vanish.

H. WAYNE TOBIN, M.D.
Chief of Psychiatry
Mid-Maine Medical Center
Waterville, Maine 04901

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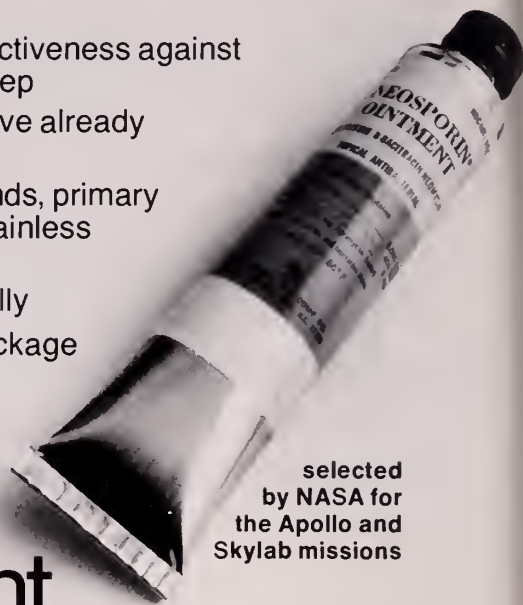
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ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

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The CO₂ Laser in Otolaryngology

LORING W. PRATT, M.D., F.A.C.S.*

The CO₂ laser has become one of the most useful and versatile instruments in the practice of laryngology. The term LASER means, **L**ight **A**mplification **S**timated by **E**mission of **R**adiation. It produces a beam of coherent light which is converted to intense heat on contact with any medium which absorbs the light. The beam can be controlled with pinpoint accuracy as to size, direction and duration of exposure so that accurate control of the application of its thermal energy to tissue is readily accomplished.

The beam from the laser travels like a rod and does not spread out like light emanating from a point source, which obeys the Inverse Square Law. All of the light energy emitted by the laser travels in an essentially parallel beam, consisting of monochromatic light with little variation in wavelength and virtually no spread in diameter. It carries great amounts of energy and is intensely hot, when converted to heat.

The production of laser light is dependent upon a change in the orbit of electrons rotating about an atomic nucleus. If an electron moves to an orbit closer to the nucleus it gives off light. It is necessary for it to absorb energy to make it move to a more distant orbit or "electron shell."

Stimulation of the atom by an external excitant, such as intense light, or a high powered electrical field is necessary to make the electron move from one orbit to another. This external energy source is called a pump which excites the laser medium. Excitation of the molecules of a gas by electrical force or by intense light will cause electrons to travel from one orbit to another in their rotation about the nucleus. In the course of this change of electron orbit, light is emitted and, as it takes place in a closed tube, some of the light is caused to travel lengthwise of the tube. Front surface metal mirrors are located at each end of the tube. These are placed with precision so the light is reflected back and forth between the mirrors repeatedly. A shutter at one end may be opened to release the coherent light beam and deliver it to its target by reflecting it along a series of front surface metal mirrors positioned on an articulated arm. This beam is projected and focused so that its path is coaxial with the optics of an operating microscope and its point of impact may be adjusted to coincide with an aiming light which is directed through the microscope, and aimed by a micromanipulator. On impact with tissue, light energy is converted to thermal energy which vaporizes water contained in the tissue and destroys the tissue. By adjustment of the laser, an exact

amount of thermal energy may be delivered to the target for a predetermined length of time. It is the precision of application of thermal energy which makes the laser such a valuable tool in the treatment of lesions.

The medium which is excited to produce coherent light regulates the characteristics of the beam produced.

For example, the ruby laser produces a red light. The argon laser produces a bluish light, which traverses the cornea, anterior chamber, lens and vitreous of the eye without damaging them, producing changes only in the retina where the beam is absorbed.

The CO₂ laser utilizes a laser medium of CO₂. In practice, one part of CO₂ is mixed with 1.5 parts of N₂ and four parts of helium. The pump is an electrical discharge through the gas.

Energy from the CO₂ laser produces a surface burn and desiccates all tissue contacted.

The application of the CO₂ laser to laryngology by Jako^{1,2,3,4} and Polyani^{5,6} and its clinical application to laryngeal surgery by Strong,^{7,8} have been great advances in laryngeal surgery. These investigators have been largely responsible for introducing this instrument to the clinical setting.

The characteristics of the laser, which make it useful are:

1. intense heat
2. localized beam
3. exquisite control of size and depth of "burn"
4. hemostasis

General anesthesia⁹ is essential for laryngeal surgery with the laser. Suspension laryngoscopy with the patient intubated with a rubber tube which has been protected by a metallic foil tape, is the procedure of choice. The potential hazard of fire¹⁰ is ever present and must be avoided by preventing perforation of the endotracheal tube by the laser beam. Plastic tubes, when ignited, give off toxic fumes not produced by burning rubber tubes. Work in the posterior commissure is facilitated by removal of the endotracheal tube and use of venturi insufflation of oxygen. Caution must be utilized continually to avoid the fire hazard.

The eyes of all operating room personnel must be protected by glasses from chance reflection of the laser beam from metallic surfaces. The patient's eyes should be taped shut with a moist sponge over the eye to avoid corneal damage.

Juvenile papilloma is a most troublesome neoplastic laryngeal lesion of small children. Conventional therapy, prior to the advent of the laser, consisted of tracheostomy followed by multiple laryngoscopies and removal of the ever growing tumor with biopsy forceps. Efforts to avoid laryngeal

*Chief of Staff and Chief, Department of Otolaryngology and Maxillofacial Surgery, Mid-Maine Medical Center, Waterville, Maine 04901.

damage during this time were not always successful and at best the tumor persisted for several years, disappearing at puberty. Strong has demonstrated a high correlation between the incidence of juvenile papillomata in children and the presence of condyloma acuminata in the mother at the time of delivery.

Laser therapy of these papillomata has changed the entire clinical course of the patient. Most tumors may be adequately controlled by repeated laryngoscopy and desiccation of the tumor by the beam of the laser. This modality utilized at regular intervals will ordinarily control the tumor and obviate the need for tracheotomy.

In the treatment of other laryngeal lesions, the laser is a valuable asset. In the management of vocal nodules and vocal polyps the precision with which the removal may be accomplished without accompanying injury to the vocal cord makes this a superior technique. Because of the narrow band of injury created by the laser, adequate unaltered specimens may be obtained for biopsy.

Laryngeal cancer¹¹ in its very early stages has been successfully resected with the laser, via the endolaryngeal route. Although in general, laryngeal cancer should be treated by a more extensive procedure, there are certain early cases of laryngeal cancer where a well localized lesion may be resected with adequate margins by this technique, and the patient may be spared a more extensive surgical procedure and its accompanying morbidity.

Early malignant lesions of the tongue and floor of mouth may be resected by the laser with adequate margin and much less postoperative morbidity than with conventional surgical techniques.

Intranasal lesions may be effectively desiccated with the laser and satisfactorily managed by this modality.

Leukoplakia may be desiccated and destroyed by the laser, while preserving the underlying vital structures and providing minimal damage to normal structures.

The narrow band of tissue damage from the laser beam means that only a few cells at the edge of the laser burn are desiccated. Healing is extremely rapid because of this and post treatment morbidity is minimal and less than that of conventional biopsy technique.

The ability to reflect the laser beam from metal surfaces has resulted in the development of hand held front surface metal mirrors which may be utilized to reflect the beam onto a lesion otherwise hidden from the direct view of the surgeon, i.e., the underside of the vocal cord, the subglottic region or the nasopharynx with the same precision as that of a direct exposure. This is a useful technique for treating lesions in these obscure areas.

The use of the laser has become more common in otolaryngology, especially in laryngology, in recent years. It offers the surgeon control of an energy source with precision which has not previously been

Continued on Page 45

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Brief Summary

INDICATIONS: For the prevention and treatment of nocturnal recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis, and static foot deformities.

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PRECAUTIONS: Thrombocytopenic purpura may follow the administration of quinine in highly sensitive patients. Recovery will follow withdrawal of the medication.

Cinchona alkaloids, including quinine, have the potential to depress the hepatic enzyme system that synthesizes the vitamin K-dependent factors. The resulting hypoprothrombinemic effect may enhance the action of warfarin and other oral anticoagulants.

ADVERSE REACTIONS: Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. If ringing in the ears, deafness, skin rash, or visual disturbances occur, the drug should be discontinued.

DOSAGE AND ADMINISTRATION:

1 tablet upon retiring. When necessary, 1 additional tablet may be taken following the evening meal.

Product Information as of September, 1977

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Herniated Intervertebral Disc

An Outline of the Current Diagnosis and Management

JOSE M. RODRIGUEZ, M.D.*

The lack of a clear understanding by the general public as well as the medical practitioner of this pathological entity is becoming more apparent to me every year.

In this paper, I will attempt to give an outline which I hope will be useful to the Maine Practitioner. Undoubtedly in doing so, I will ignore the many exceptions to the general rule.

Patients with herniated intervertebral discs are treated by many different practitioners including chiropractors, osteopathic physicians, and general practitioners besides the orthopedic surgeons and neurosurgeons which are the specialists usually performing surgery for this problem. For this reason, the patient is sometimes confused by the different explanations as to the cause of the symptomatology and the different forms of management.

At the outset, I wish to emphasize that the syndrome of herniated intervertebral disc is not synonymous with the so-called chronic back.

The terms "slipped disc" is also, I believe, a misnomer as it is interpreted by many as meaning that the intervertebral discs as a whole has slipped out of place. This concept is unfortunately widely accepted by most patients and goes well with the erroneous idea that it can be put back in place by manipulation.

The terms "ruptured disc" implies the first step of the pathological process which may later produce the syndrome. I am going to refer to this, in this paper, as a herniated disc fragment.

DIAGNOSIS

The diagnosis of a herniated disc fragment can usually be made clinically. I will attempt to outline the clinical findings encountered at the different levels and types of disc herniation.

In the cervical area, the most common locations for a disc herniation are at the C5-6 and C6-7 level, although many occur from C2-3 to C7-T1. Cervical disc herniation most commonly occurs posterolaterally but can also be central. In the posterolateral disc herniation, the symptomatology would manifest itself as a nerve root compression syndrome with special characteristics depending on the level involved. In the case of a C5-6 posterolateral disc herniation, compression of the C6 root would occur and this would produce weakness of the biceps muscle, diminished or absent biceps reflex and sensory changes involving mostly the thumb. At the C6-7 level, the fragment of disc will produce a compression of the C7 nerve root with weakness of the triceps muscle, ab-

sent or diminished triceps reflexes and sensory changes mostly in the index and middle fingers. The less common sites at C3-4, C4-5, and C7-T1 will also produce changes according to the roots involved. The C4-5 may also produce biceps weakness and diminished biceps reflex, but the sensory distribution will be closer to the deltoid area and arm. The C7-T1 will involve the fourth and fifth fingers, etc. In all cases, the general symptoms of a cervical disc herniation will be limitation of extension of the cervical spine with a positive foraminal compression test, that is extension and lateral rotation of the head to the opposite direction will bring on radiating pain into the affected arm.

Another maneuver that would increase the severity of the pain would be an increase of the intraspinal fluid pressure which is produced when straining, coughing, and sneezing. The patient also finds that it is difficult for him to rest in a supine position because of venous congestion which usually increases the severity of the pain. Many times, they have to sleep in a recliner. The less common central disc protrusion may just produce neck pain and limitation of motion of the cervical spine, but if the fragment is large enough it may produce cord signs and could be mistaken for a spinal cord tumor.

X-rays of the cervical spine may only show a straightening of the cervical lordosis due to muscle spasms, but if the patient has had previous neck problems, he may show already a narrowing of the intervertebral disc space. The clinical diagnosis of a herniated cervical disc usually need confirmation by cervical myelography. Occipital headaches are usually present in central disc herniations.

The dorsal disc protrusion is rare and could produce a spinal cord compression or dorsal root signs. Differential diagnosis in this particular case is with spinal cord tumor. The average practitioner would rarely see a typical dorsal disc herniation.

The most commonly seen disc herniations are in the lumbar area. The onset of the symptomatology is usually acute and may occur in a patient with previous history of back problems and may follow manipulative therapy. In a patient that has had discopathy for a long period of time sometimes a trivial circumstance such as sneezing, or straining, or minor lifting or sitting for a prolonged period of time such as a long car trip may precipitate the herniation of a fragment.

The most common cause of a ruptured disc with eventual herniation is produced by lifting usually in an awkward position or by sudden rotation of the spine while lifting. In the female, the most common cause of a ruptured disc is at the time of delivery of a child.

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In most cases the first symptoms are severe low back pain with muscle spasms which is soon followed by radiation of the pain into one hip and down into the leg. This pain is always increased by straining, coughing, and sneezing and many times made worse by applying any weight on the affected leg or sitting or attempting to lift. It is usually helped by bed rest and by flexion of the thigh on the abdomen. In many cases after a while the back pain subsides and only the leg pain persists and becomes more apparent to the patient. Sometimes the patient could notice association of sensory and motor changes involving that leg.

At examination the patient usually has marked limitation of motion of the lumbar spine especially flexion and there is evidence of paraspinal muscle spasms with a tilt or list to one side which is increased when attempting to flex the spine. Straight leg raising is usually very painful in the affected side and at times when a fragment is impacted in the foramen or at the axilla of the nerve, the straight leg raising in the opposite leg will also produce pain on the affected side. The patient also finds that it is difficult for him to get dressed especially to put his shoes and socks on. Another symptom commonly complained by the patient is the increase of severity of pain when attempting to put any weight on that leg.

Depending on the level of the disc herniation, there are specific motor and sensory changes. At L3-4, there is evidence of nerve root deficit of the L3 root manifested by a diminished or absent knee jerk and sensory changes mostly in the anterior thigh and knee and occasionally when the L4 root is involved on the inner aspect of the leg. There is also usually weakness and eventually atrophy of the quadriceps muscle.

When the herniation occurs at the L4-5 level, there is evidence of L5 root deficit manifested by weakness of the dorso-flexor of the big toe or even a foot drop and sensory changes over the dorsum of the foot and big toe and occasionally over the lateral aspect of the calf.

In the L5-S1 disc herniation, the patient shows an absent or diminished ankle jerk and the sensory changes over the outer aspect of the foot and the fourth and fifth toes. There is weakness of the flexors of the toes and sometimes weakness and atrophy of the gluteal muscles.

A massive disc herniation may produce cauda equina syndrome with urinary and bowel involvement and sensory deficit which may encompass several roots.

Once a diagnosis of a herniated disc is made clinically it may be advisable to proceed with myelography to determine the size and location of a herniated fragment. Recently water soluble iodine compounds are being used which makes myelography much easier on the patient.

MANAGEMENT

Because a patient with a herniated disc fragment either cervical or lumbar is in very acute and severe

discomfort, I believe that hospitalization should be advised.

In cervical disc, cervical traction plus the use of anti-inflammatory compounds plus moist heat and ultrasound therapy should be tried first. Analgesics may be necessary because of the severity of the pain. If a disc fragment is sequestered, the medical management is usually not successful and then surgical management should be considered without undue delay. Only if the pain is controlled with medication and there is no progression of the neurological deficit more prolonged conservative management is justified. If the symptoms are limited to only arm pain without neck pain, posterior approach with removal of the herniated fragment and decompression of the nerve may be the procedure of choice. However, if the herniated fragment by myelography is large and there is also quite extensive neck pain, the anterior approach would be recommended. In my experience, this procedure is very well tolerated and the herniated fragment can be found and removed even if it has extruded into the canal. I usually proceed with an interbody fusion and in my own practice, I have found that the results are better than when done without fusion. The symptoms are usually controlled fairly rapidly and the patient may be free of pain within a few days following surgery. A recurrence of a disc herniation in the neck is rare and when symptoms recur, it is usually due to herniation at another level.

In the lumbar area, the treatment should consist of bed rest, moist heat, ultrasound and anti-inflammatory compound plus muscle relaxants and analgesics. Traction in lumbar discs in my experience is not effective.

After two weeks usually the inflammatory changes produced by the disc herniation are reduced and the symptoms start to clear when they are going to respond to conservative management. However, if the symptoms persist or there is further evidence of neurological deficit, I believe that surgery for the removal of the extruded fragment is indicated without undue delay.

Surgery should consist in exposure of the nerve root involved and removal of the disc fragment without sacrificing the architecture of the spine. This should be done using magnification and adequate lighting and with special instrumentation for this purpose.

The use of extensive bone removal or large decompression of the spine or a spinal fusion is not indicated for this particular type of syndrome.

Removal of the extruded fragments brings immediate relief of the leg pain even on the day of surgery and the patient could be discharged from the hospital in two to five days. Ambulation can be started the day of surgery and back strengthening exercises are recommended immediately following discharge.

A recurrence of a disc herniation in the lumbar

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Indications for Computed Body Tomography

ALBERT A. POULIN, M.D.

Computed Tomography was introduced in 1972, but respiration suspended body computed tomography was not possible until late 1975. Most C.T. units originally confined to head scanning (HCT) but acquisitions in the last two years of C.T. units have shown a preponderance of body devices (BCT) because of their versatility. The reluctance of government agencies to pay for a new technology when they have yet to understand the old ones has led to many attempts to regulate the use and acquisition of C.T. scanners. Various attempts have been made to secure the aid of groups of interested parties to a reasonable consensus of utilization of B.C.T. scanners now in operation.

The Society for Computed Tomography published such guidelines in July 1979 and a brief outline in condensed form is reviewed.¹

Neck

- 1—Extent of primary and secondary neoplasm of the neck
- 2—Evaluation of body abnormalities of the cervical spine
- 3—Locating foreign bodies in soft tissue and airways
- 4—Evaluation of retropharyngeal abscesses

Mediastinum

- 1—Mass
 - Differentiation as to cystic, fatty or solid nature
 - Relationship to other mediastinal structures
- 2—Mediastinal widening
 - Assessment of pathologic or anatomic widening
 - Distinction of solid masses, vascular anomaly or aneurysm
- 3—Hilum
 - Pulmonary artery from solid mass
- 4—Paraspinal line widening
 - Lymphnode enlargement, vascular structure or variant

- A. Search for occult thymic lesion
—Thymoma or hyperplasia in patients with myasthenia gravis

Lung

A. Search for pulmonary lesions

- 1.—Detection of pulmonary metastases when extensive surgery is planned with high propensity for lung metastases or apparent single metastasis
- 2.—Positive sputum cytology with negative chest films and bronchoscopy.
- 3.—Assessment of lung underlying pleural effusion or post pneumonectomy.

- B. Search for central calcification in pulmonary nodules with conventional tomography indeterminate

- C. Extent of intrathoracic spread in selected cases of bronchogenic carcinoma.

Chest Wall

- Determination of extent of neoplastic disease

Heart

- Not indicated at this time

Major Blood Vessels

- Evaluation of thoracic and abdominal aortic aneurysms.
Evaluation of grafts of major vessels including disruptions

Spine

- 1—Evaluation of spinal stenosis
- 2—Dysraphic abnormalities
- 3—Evaluation of bony or paraspinal tumors or inflammatory masses

Retroperitoneum

- 1—Detection of primary malignancies
- 2—Nodal extension of lymphomas and other types of malignancies
- 3—Detection of abscess or hemorrhage

Peritoneum

- 1—Detection of free or loculated fluid collections or abscesses
- 2—Detection of peritoneal masses

Liver

- 1—Evaluation of space-occupying lesions
- 2—Evaluation of trauma
- 3—Evaluation of diffuse liver disease if of limited value

Spleen

- 1—Detection of subcapsular hematoma
- 2—Detection of intrasplenic masses

Pancreas

- 1—Evaluation for possible mass lesion
- 2—Differentiation from pancreatic and parapancreatic mass acute or subacute pancreatitis

Kidneys

- 1—Evaluation of kidneys when patient is allergic to contrast media
- 2—Evaluation of renal mass found on another imaging procedure
- 3—Evaluation of para or perirenal lesions
- 4—Evaluation of nonfunctioning kidney
- 5—Evaluation of renal and perirenal calcifications
- 6—Assessment of renal trauma

Gallbladder—not indicated at this time

Biliary tree

- 1—Differentiation of obstructive from nonobstructive jaundice

- 2—Determination of site and etiology of obstruction

G.I. Tract

- 1—Not indicated for mucosal lesions
- 2—Useful for extension of tumor into mesentery

Adrenal Gland

- 1—Evaluation with biochemical evidence of adrenal hyperfunction
- 2—Evaluation of patients with suspicion of adrenal mass on conventional examination

Uterus and Ovaries

- 1—Evaluation of mass or staging after biopsy
- 2—Evaluation of primary tumor and extent of spread (usually after failure of ultrasound examination)

Bladder, Ureters, Prostate

- 1—Evaluation of primary and secondary tumors
- 2—Differentiation of solid, cystic and inflammatory masses

Musculoskeletal System

- 1—Evaluation of patients with bone tumors
- 2—Evaluation of patients with recurrent tumors
- 3—Evaluation of patients with soft tissue tumors

Therapy Planning and Followup

- 1—Dose planning and attenuation coefficients of bone and soft tissue in tumor-bearing areas for planning radiation therapy
- 2—Base line studies prior to treatment from which effectiveness of treatment by radiation therapy or chemotherapy can be judged

Obviously such a long laundry list of potential use does not mean that all patients with these conditions would benefit by referral to a body scanner. In some cases nuclide or ultrasound studies may be adequate to confirm a diagnosis and in some may be superfluous.

Our experience with an E.M.I. 5005 general purpose scanner installed and operational since June 1977 has gone through several periods of adjustment. Initially all budgeted time was given to head scanning. Body scans were only scheduled when available time was not needed for head scanning. During our initial six month period BCT only averaged 5-10% of the patients who were examined. We quickly found that BCT also was very time consuming and necessitated careful evaluation of the patient and supervision of various portions of the study. Our original attempts were confined to screening the entire abdomen on usually very ill patients. In spite of an 18 second sweep, many of these patients could not suspend respiration and the motion artifacts were substantial. Contrast studies were added to delineate structures within the abdomen and drugs given to decrease peristalsis. Our average time for these studies approximated 2-3 hours machine time per patient.

As we gained more expertise we found that studies directed to a specific area with special manipulation

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- Convenient bedtime dosage.
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Brief Summary

INDICATION

Nausea and vomiting of pregnancy.

PRECAUTIONS

Because of potential drowsiness, Bendectin should be prescribed with caution for patients who must drive automobiles or operate machinery. Studies in rats and rabbits have revealed no suggestion of drug-induced fetal abnormalities at doses of Bendectin up to 90 times the maximum human dose. In addition, several epidemiologic studies in women who received Bendectin during pregnancy have shown that the incidence of birth defects in their offspring is no higher than in women not taking the drug during pregnancy. Nevertheless, like all drugs considered for use during pregnancy, particularly during the first trimester, Bendectin should be used only when clearly needed.

ADVERSE REACTIONS

The adverse reactions that may occur are those of the individual ingredients. Doxylamine succinate may cause drowsiness, vertigo, nervousness, epigastric pain, headache, palpitation, diarrhea, disorientation, or irritability. Pyridoxine hydrochloride is a vitamin that is generally recognized as having no adverse effects.

DOSAGE AND ADMINISTRATION

2 Bendectin tablets at bedtime. In severe cases or when nausea occurs during the day: 1 additional Bendectin tablet in the morning and another in midafternoon.

Product Information as of January, 1978

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of contrast agents and computer data increased our quality of scans and resulted in more accurate data. Improved software updating by the manufacturer, addition of hard copy films and technical improvements resulted in consistent reproducible quality.

By the second year, our referrals for body scanning were substantially increased in spite of a larger total patient work load. At the present time (3rd year) BCT approximates 15-20% of the work load of 140-150 patients per month. Most BCT scans average two hours per procedure as compared with one hour for a HCT scan done as a double procedure with and without contrast. Complicated procedures covering several organ systems or body areas still take an inordinate amount of physician time and input if an optimum study is to be done.

Statistics

1977-1978	—	Total patients	1015	BCT's	101
1978-1979	—		1476		188
July 1, 1977-Oct. 31, 79			565		86
Distribution of Body Scans (last 100)					
Neck		10%		
Abdominal and pelvic		62%		
Spine		12%		
Chest and mediastinum		8%		
Misc.		6%		
Mixed		2%		

In our experience, body scanning has been most helpful in the areas not amenable to conventional studies or in which body computed tomography is a singular modality with no comparable other study available (a good example of this is spinal studies for spinal canal stenosis.) The percentage of positive findings are extremely high in the neighborhood of 60 + percent in all body scans due to careful screening and the presence of known serious diagnosis such

as malignant disease when the patient was referred.

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THE CO₂ LASER IN OTOLARYNGOLOGY—Continued from Page 40

available for surgical work. This has permitted laryngeal surgery, especially, to be performed with greater accuracy and more complete hemostasis than ever before. Its application to recurrent juvenile laryngeal papillomata has been one of the greatest advances in laryngology in recent years.

Reports have been made of the value of the laser in making myringotomy openings which stay open longer than otherwise would be the case. Some middle ear lesions have yielded to the laser beam, but its use in otology has not yet been thoroughly explored.

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Intraoperative EEG Monitoring During Carotid Endarterectomy

MARVIN A. EISENGART, M.D.* AND JOHN W. TOWNE, M.D., F.A.C.S.**

It was 25 years ago that Eastcott, Pickering and Rob¹ first described the surgical treatment of symptomatic extracranial vascular disease. Since then numerous studies have established carotid endarterectomy as one of the principal modes of therapy for relief of cerebral ischemia and prevention of stroke. Two major problems persist: (1) the proper selection of patients for surgery, and (2) the employment of techniques to reduce the risks of the surgical procedure.

The present report relates our experience with intraoperative EEG monitoring during carotid endarterectomy carried out on 30 patients during the past 3 years. All of the patients presented with one or more of the following symptoms and/or signs: amaurosis fugax, transient neurological deficits referable to the carotid arterial distribution of a cerebral hemisphere, or a completed stroke in a similar distribution but which had cleared to leave no more than a mild residual neurological deficit. These patients were examined neurologically and had several studies performed including EEG and radio-nuclide or more recently CT scan of the brain. Arteriography revealed 50% or in most cases greater narrowing of the carotid artery appropriate to the side of symptoms. Ulcerations of the carotid artery were present in some patients but were not the sole criterion for deciding to operate. These clinical and arteriographic criteria are those generally agreed upon as indications for endarterectomy.^{2,3} The patients also had no major medical contraindications to surgery.

METHODS

Preoperatively the patients had standard EEG electrodes (Grass gold cup) placed symmetrically at frontal, central, anterior temporal, mid-temporal, and occipital locations. Contact was made with conductive jelly and the electrodes were held in place with collodion-soaked gauze squares. The electrodes were connected to a Grass Model 8 EEG machine through a protective patient isolation input device. Recording was made at paper speeds of 30 mm/sec. (standard speed) and 15 mm/sec. The EEG montage used was that of Sharbrough, et al.⁴ Recording commenced at the time of anesthesia induction (halothane was used) and continued throughout the surgical procedure until skin closure.

RESULTS

All but 5 of our patients had normal preoperative routine EEG's. Under anesthesia, the pattern exhibited by the patients was as reported⁴ dominated by activity in the alpha frequency range (8-12 Hertz) with superimposed faster and slower frequency activity. The 2 patients with asymmetry of their preoperative recordings also showed similar asymmetry of the halothane induced rhythms under anesthesia. The side that was slower preoperatively tended to show more slow activity under anesthesia. During surgery, the overall pattern of the EEG was found to vary with the depth of anesthesia and to a lesser extent with blood pressure. A drop in blood pressure could produce diffuse slowing of the EEG; therefore, the anesthetist tried to maintain the patient's normal blood pressure throughout the procedure, using vasopressor agents if necessary. The variation in the EEG as a result of increasing anesthesia concentration was also in the direction of showing more slow activity in the theta and delta range and to diminish the alpha and faster frequency activities. When this occurred, the anesthetic concentration was reduced and the EEG returned to a faster background rhythm.

When the carotid artery had been exposed and cross clamping took place, 24 patients had no changes in the EEG at that time or throughout the entire surgical procedure. In 6 patients, there were marked and rapid changes in the EEG on the side ipsilateral to the clamped artery. In those patients, the EEG showed dramatic flattening and attenuation of the rhythmic alpha and fast frequency activity previously present. In its place were low voltage, slow or indeterminate frequency activity (See Fig. 1). As soon as these EEG changes were recognized (from 5 to 30 seconds after clamping), the surgeon placed a Javid shunt in the artery and proceeded with the endarterectomy. The EEG would gradually return to its pre-clamp symmetry generally within 30 to 120 seconds after reestablishment of flow (See Fig. 2). Later upon reclamping the artery at the time of removal of the shunt, 5 of these 6 patients had recurrence of the EEG changes seen at initial clamping. These changes reverted to normal after reestablishment of flow through the repaired carotid artery. In this instance, the return to normal took as long as 10 minutes in one patient. All of these five patients had had sluggish back bleeding from the stump of the distal portion of the carotid artery following clamping and arteriotomy. The sixth patient who had had no EEG slowing at the time of shunt removal, but who did have slowing at the time of initial clamping, also had demonstrated good back bleeding at the in-

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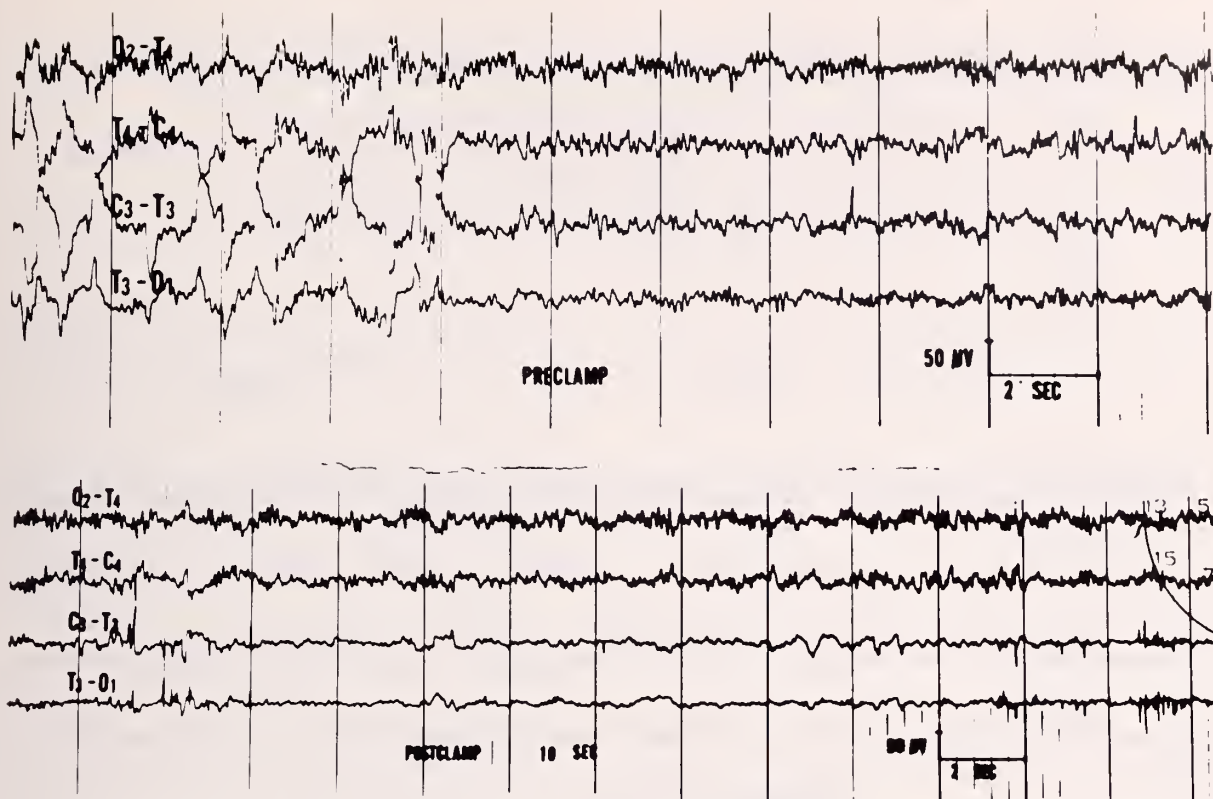


Fig. 1. In this and the following Figure, the EEG's are labeled according to their derivations from occipital (O), mid-temporal (T), or central (C) derivations. The even numbers (the top two channels of each group of four) refer to the right hemisphere and the odd numbers refer to the left. In the first recording labeled "Pre-clamp," it can be seen that the top two channels representing the right hemisphere and the bottom two channels representing the left hemisphere show symmetrical EEG activity. The bottom recording labeled "Post-clamp" is taken 10 seconds after occlusion of the left common carotid artery. It demonstrates that the two lower channels recording from the left hemisphere have a marked attenuation of the faster frequency activity (the sharper appearing waves) compared to that on the right.

itial arteriotomy. It was felt, therefore, that the EEG slowing seen at first clamping in this patient may have resulted from embolization of atheromatous debris caused by manipulation of the carotid bifurcation.

None of the patients whose EEG's dictated use of the shunt had any postoperative neurological sequelae. Two of the other 24 patients did suffer mild strokes postoperatively. Their EEG's remained symmetrical and unchanged throughout the endarterectomy. They were intact coming out of anesthesia, but several hours later neurological deficits suddenly developed. In one patient an arteriogram done immediately afterward showed a widely patent artery with no narrowing or thrombosis at the operative site. Both patients made essentially complete recoveries.

DISCUSSION

When the carotid artery is clamped for the endarterectomy, the ipsilateral cerebral hemisphere is dependent upon collateral circulation for its blood supply. Preoperatively the arteriogram can identify those who are at risk for having insufficient collateral flow, such as those with occlusion of the contralateral carotid artery or with severe diffuse vascular disease. In these patients, one might elect beforehand to use an indwelling shunt to circumvent the prob-

lem. Some centers use a shunt for all their endarterectomies; however, this is not entirely without hazard.⁵ Shunt tubes can "...cause intimal damage resulting in thrombosis, disruption of the plaque with embolism, or introduction of air into the carotid system..."⁶ It is estimated that the shunt is actually needed in only 10%-20% of patients; therefore, one would like a physiologic test for determining who those patients are.

Other techniques for prophylactically increasing cerebral blood flow during endarterectomy including hypercarbic general anesthesia and induced systemic hypertension have been employed, but the results are not uniformly successful. This does not remove the need necessarily for the use of an indwelling shunt. Measurement of the pressure in the "stump" of the carotid artery distal to the clamp has been done, but here, too, there are instances in which the stump pressure and cerebral blood flow show poor correlation. The shunt, however, is the only means of delivering adequate amounts of blood to a hemisphere which has inadequate collateral circulation.

Studies by Sundt, et al⁷ and Trojaborg and Boysen⁸ have established the existence of a high correlation between cerebral blood flow measured by intra-arterial Xenon-133 and changes in EEG activity. In both studies, it was demonstrated that flattening of the EEG (such as seen in our patient in Fig. 1)

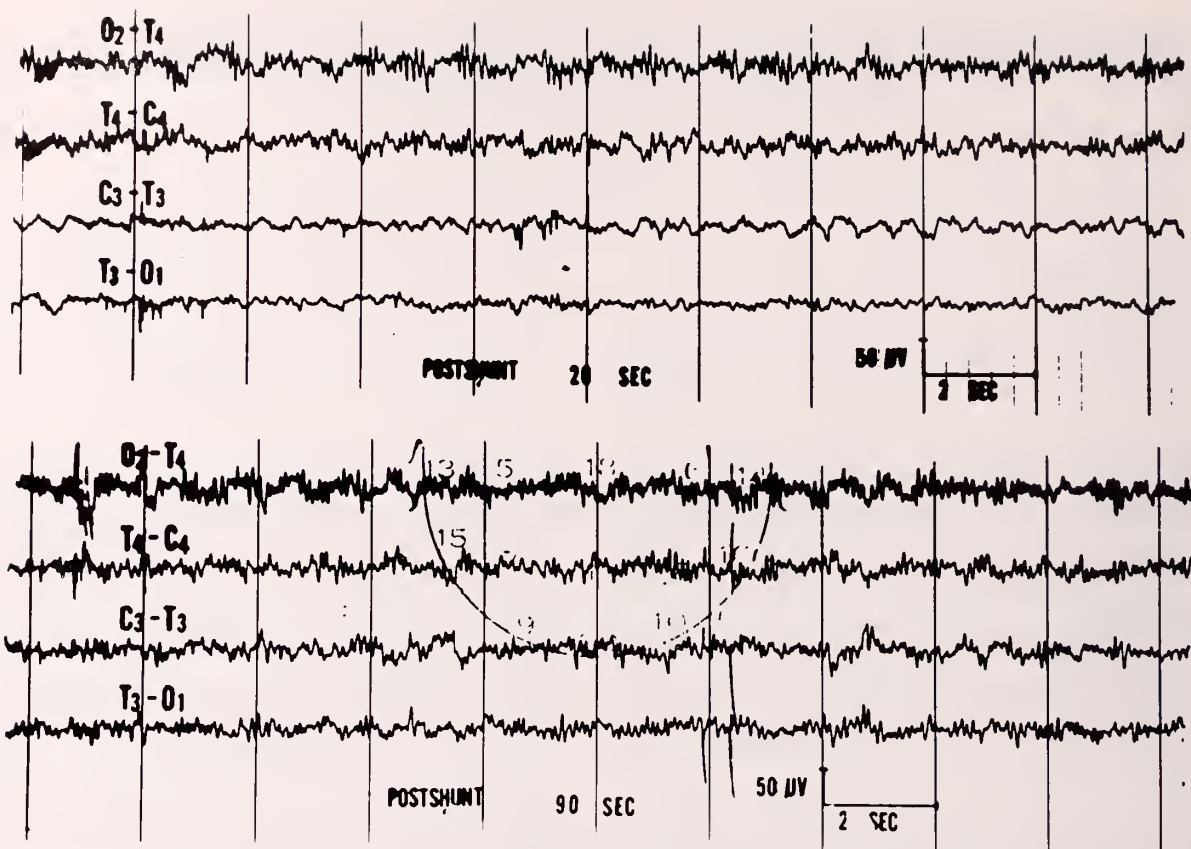


Fig. 2. The two sets of recordings are from the same patient seen in Figure 1. The top set labeled "Post-shunt 20 seconds" shows an asymmetry with relatively less fast activity seen in the lower two channels from the left hemisphere, but nevertheless some improvement when compared with the immediate post-clamp recording in Figure 1. The lower set of recordings labeled "Post-shunt 90 seconds" shows a return to symmetrical activity in the left hemisphere so that the lower two channels and upper two channels now appear symmetrical as they did in the pre-clamp state in Figure 1.

occurs with cerebral blood flow below 17-18 ml/100 gm/min. With cerebral blood flow of approximately 20 ml/100 gm/min., there was slowing of the EEG without dramatic flattening in a few patients.⁸ With any blood flow above that level, there is for the most part no change in the EEG during the time of surgery. Clinical experience has dictated that with maintained normal "halothane" EEG activity during the period of time required for endarterectomy, the cerebral hemisphere appears to tolerate whatever degree of relative ischemia might be produced by ipsilateral carotid clamping during surgery. If the EEG becomes abnormal, it is because of a drop in flow below the critical levels just noted above, or as in one of our patients (and in others reported in the literature) because of probable cerebral embolism during manipulation of the artery.

Studies reported in the literature as well as our own much smaller experience have convinced us that the EEG is a readily applied, reliable method for assessing the physiological state of the cerebral hemisphere during carotid endarterectomy. It provides information indirectly regarding the depth of anesthesia, blood pressure, blood flow and carbon dioxide concentration in the blood. Most importantly, it guides

the surgeon in selecting those patients requiring indwelling shunts during endarterectomy and excluding those who can withstand surgery without them.

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Fine Needle Aspiration Breast Biopsy

A Six-Year Experience With 1034 Aspirations*

GEORGE F. SAGER, M.D., LOUIS N. TAXIARCHIS, M.D.
AND BARBARA H. BOWDOIN C.T. (ASCP) (IAC)**

Fine needle aspiration of breast lesions is a valuable step in planning the care of the patient with a breast lump. Since adopting this procedure in 1973, our experience with 1034 breast aspirations reveals that when performed correctly, and properly interpreted, the results are rarely misleading. A smear revealing ductal cells and free of artifacts is necessary to provide reliable information. A negative cytologic study should never dissuade the physician from biopsying a suspicious mass.

CLINICAL MATERIAL

We reviewed 1034 breast aspirations, most of which were from solid tumors. Cytology studies positive for carcinoma were reported 128 times and all but 2 were confirmed by pathologic material. The 2 false-positives were in a 90-year-old man with gynecomastia, and a case of sclerosing adenosis read very early in our series that would now not have been called positive. A false-positive rate of 1.5% of all positives or 0.2% of all smears is reassuring.

There were 33 instances where carcinoma was found at biopsy but the smear was negative or unsatisfactory. The positive path reports were recovered by searching the reports of breast cancer from the pathology departments of the hospitals in the Portland area. This yields a false-negative rate of 3%.

A review of patients in whom smears were reported as suspicious revealed that of 54 such reports, 37 (69%) had proven carcinoma; 15 (28%) had negative biopsies, and 2 (3%) had no follow-up. One of these two refused biopsy and died of other causes and the other was lost to follow-up. In this institution, a suspicious report is interpreted as positive until proven otherwise.

Thirteen percent of the smears was deemed unsatisfactory because of absence of ductal cells or poor preparation. The absence of ductal cells may be caused by inadequate sampling which may be avoided by multiple passes of the needle through the tissue, or by the acellular nature of some fibrous masses. The poor preparations usually involved a drying artifact which can best be avoided by immediate spray fixation of the smear. The clinician must never interpret an unsatisfactory report as a negative report. It

TABLE 1

VARIATION IN RESULTS AMONG DOCTORS

Dr.	Total Asp.	Pos.	Susp.	Unsat.	% Unsat.
1	179	14	8	26	14
2	175	1	6	22	12
3	158	49	15	5	3
4	83	6	8	19	22
5	77	15	7	13	16
6	39	1	0	6	15
7	38	1	0	10	25
8	26	9	2	4	15
9	14	4	1	2	14

should be interpreted as "no test" and repeated aspiration considered.

A review of the experience of individual doctors is outlined in Table 1 and reveals significant variations. Dr. #2 usually submits fluid from breast cysts and his yield for carcinoma is very low. Dr. #3 almost never submits fluid from cysts and his yield of positives is much higher. His low rate of unsatisfactory smears is explained by his particular interest in the procedure.

DISCUSSION

Most reports confirm the safety and reliability of aspiration biopsy of breast masses. Many hospitals report experiences very similar to ours.^{1,2,3,4,5,6} Except for one study from England⁷ with totally unsatisfactory results, the false-negative rate is 2-5% and the false-positive reports are 0-0.3%. When correlated with the clinical examination and the mammographic findings, if all three are positive, the diagnostic error is less than 1% and definitive treatment may be undertaken without further biopsy.⁸

The initial report of fine needle aspiration of breasts from our institution⁹ suggested this would be a useful procedure and now with over 1000 aspirations it continues to be simple, safe and reliable.

SUMMARY

The cytologic study of fine needle aspiration of breast masses is now established as a safe, simple, rapid and reliable method to hasten the diagnosis and treatment of breast lesions. A six-year experience with 1034 aspirations produced 0.2% false-positive and 3% false-negatives. The technical quality of the smear is important and recommendations are made regarding the interpretation of unsatisfactory smears and steps to reduce their occurrence.

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*Presented at the Tenth Annual Surgical Symposium of the Maine Medical Center, Portland, Maine, March 30, 31, 1979.

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Diagnostic Imperatives In Internal Medicine

The Timely Detection of Treatable Disease

The Periodic Health Examination

SAMUEL PROGER, M.D.*

INTRODUCTION

Patients may be free of symptoms yet have a serious though curable disease—a bowel or breast tumor for example. Or, they may have ignored the early symptoms or physical changes of a disease that is curable if diagnosed and treated early. Such diseases will be discovered only on a routine health examination of the apparently asymptomatic patient. Hence, the justification for the periodic health examination. And hence, the reason for including this chapter in a book dealing with diagnostic imperatives.

The annual physical examination has come under increasing attack in recent years. Some objectives stem from the sheer cost of such examinations (\$50 to \$500 each) when performed indiscriminately. The critics also question the value of the annual physical checkup in cost-benefit terms.

The story is all too familiar about the patient dropping dead of a heart attack just after being given a "clean bill of health" in his annual physical examination. A study of 350 patients who had been enrolled in a periodic health examination program at the University of Pennsylvania a few years ago indicated some justification for the story. It was found that the disease that eventually proved fatal went unrecognized in 40% of the cases, even among patients who had their periodic examination in six months before death.

It is not only statisticians and students of health care who question the value of comprehensive annual checkups today. As patients grow increasingly sophisticated, they, too, are concerned about the value of the periodic examination. If the patient believes that a periodic health examination can result in detection of even a small percentage of diseases that can be controlled or cured by early diagnosis, he or she wants to be included. On the other hand, if unnecessary or marginal tests are going to increase out-of-pocket or insurance costs he is directly concerned.

It seems apparent today, after a century of encouragement of periodic health examinations, that there is no unequivocal proof of their value when viewed from a cost-benefit perspective except in infants and children; this despite the economies resulting from the growth of paramedical personnel and the development of automated means of acquiring

data. This is not to say that periodic meetings between physician and patient have no use. Such meetings can be very productive in developing programs to promote well being, to establish rapport between physician and patient and to provide basic information from which the physician may make value judgements on what tests may be needed.

One trend seen today is for patients to assume a greater share of responsibility for their own health, in accordance with suggestions made by the physician. Such programs can include the carrying out of some simple tests at home, certain types of self-examination (breast, skin, testes, neck and mouth), diet and exercise regimens plus periodic meetings with the physician. The physician and patient may wish to work out a schedule in which the limits of self examination would be decided and the conditions for a return to the doctor's office spelled out. This kind of arrangement requires, of course, rapport between physician and patient, and mutual trust. The frequency of visits and the extent of self care would take into consideration the patient's age, presence or absence of chronic conditions, general health and the patient's disposition and outlook on life.

This last consideration is important in the minds of many—physicians and patients alike—for it is popular now to criticize the treating of diseases per se and to urge treatment of the "whole person." Many physicians, of course, always have practised what today is called "behavioral medicine," considering a patient as a unified mental and physical being.

Functions of the Periodic Health Examinations

Periodic visits with a physician appear to be an important part of all types of practice, whether one calls it specialization, behavioral, holistic, or by any other name. While there may be no magic in setting up regular physical checkups, it is important for patient and physician to establish and maintain some personal contact while the patient is asymptomatic. Then the physician is better able to judge changes in the status of the patient's health and to decide what tests should be ordered.

Patient visits can be very helpful from two other points of view. Consider first, the patient who presents himself for a periodic examination and appears to be healthy, is cheerful in outlook on life, and is trying hard to follow a life style that would minimize the occurrence of those diseases that may be delayed or avoided by prudent living. Such a pa-

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tient can be encouraged to continue his efforts. He can be reassured about the state of his health. He can be sent away with renewed determination to avoid indulging in harmful practices, and to continue to discipline himself. On the other hand there is the patient who has not been living sensibly. He is probably more inclined to take advice from a physician to change his ways than he is to accept criticism from spouse or friends who try to tell him to stop smoking, or that he is becoming obese or drinking too much.

With a sound doctor-patient relationship, these two patients may be given a minimum of tests. The big contribution of the physician in each case is that of either giving reassurance to the person doing well or a warning to the one who is too lax.

Neither of these functions requires a great deal of the physician's time. The doctor may order certain limited tests to monitor physical functions, but often these can be done through multiphasic screening or by technical personnel. The personal contact, although limited, seems essential because the patient, no matter how self-reliant he may appear, can gain from the meeting with the physician and from either the reassurance or the warning he may receive.

The extent of tests remains a matter of judgement, and this is an area where the waters become more muddled. Since the purpose of a periodic health examination is to prevent disease, to detect it in its early and curable stage, or delay its onset or progress if it is not preventable, the examination may be looked at as a search for findings that would, if not discovered, lead to unnecessary or at least earlier disease. Additional concerns include the rarity and seriousness of the conditions one may uncover—again raising the question of cost-benefit considerations. For example, the cost per case of finding high blood pressure on a routine examination is small, but the condition is serious and can be effectively treated. On the other hand, while the cost of a single chest x-ray is also relatively small, the cost per case of detected treatable disease is high. The chest x-ray, thus, unlike the blood pressure measurement, might more readily be questioned in a cost-benefit analysis of a community screening study. But in the office of the practising physician, the patient is a person and not a statistic and even if the findings are negative, wants to be reassured as to the state of his health. To be able to report negatives and hence to provide reassurance and peace of mind is a major achievement in promoting health. It is, after all, an important contribution of the physician, as it has been for "healers" everywhere and in all societies since time immemorial.

The importance to a patient of a negative "outcome" is illustrated further by the following quotation from McDermott:

"...the examination of a small lump in a woman's breast may involve the use of a considerable amount of complex technology (mammography, xeroradiography, thermography, anesthesiology, surgery, tissue microscopy). After the use of all that technology, the outcome is that the patient turned

out not to have cancer.

Considered solely in terms of the public good, one might argue that this not inconsiderable effort was wasted. After all, if the woman had done absolutely nothing about the breast lump and forgotten all about it, she would have been just as well off. The investment in money and effort had no demonstrable influence on her or the people's health. Yet all of this effort is essential to fulfill the doctor's primary purpose to help the patient toward peace of mind. This highlights that ever recurring problem of the difference between the public good and one's own."¹¹

There may be beneficial biologic effects of reassurance; whether from the report of negative findings, or from placebos. These effects may be substantial and perhaps even profound. When a patient in a sickbed says that he or she feels better just as soon as the doctor walks into the room the patient is describing biologic effects and health benefits which we have not yet measured adequately. We now know for example that a sharp increase in the secretion of epinephrine from the adrenal glands such as can occur with severe fright can prove fatal in patients with acute coronary heart disease. The patient can literally be frightened to death. If the biologic effects of emotions are known to be harmful in one direction (fright-anxiety), they may be found to be helpful in the opposite direction (reassurance and peace of mind).

As noted earlier, a periodic examination offers regular opportunities to reinforce health advice. Health advice can be made especially forceful if for example weight gain is associated with increasing blood pressure or blood sugar, if cigarette smoking has resulted in substantial lowering of pulmonary vital capacity, or if alcohol intake has produced early evidence of liver damage. Those who find it difficult to resist the powerful human impulses for self-indulgence may require equally powerful incentives to check these impulses. Periodic examinations that reveal new and asymptomatic but disturbing changes may provide such incentives.

Comprehensive or Targeted Periodic Examination

The periodic examination does not need to cover everything for everybody at every examination. The examination can be targeted to individual circumstances. In a heavy smoker an annual x-ray of the lungs is desirable. Otherwise, in the healthy non-smoking asymptomatic adult, with no other high risk environmental exposure, the annual chest x-ray may be omitted.

Spitzer and Brown² ask the question: "Are asymptomatic persons who solicit a periodic health examination different in health status from persons in whom the checkup is professionally imposed?" The question, though important, is unanswered in terms of customary health statistics. The yield of "significant findings" in health checkups gives us no information, for example, as to the yield of benefits from reassurance. Yet those who solicit the health appraisal are more likely to need reassurance.

For those who do not solicit the checkup but on whom it is professionally imposed, we cannot be certain that an asymptomatic and apparently healthy person is truly healthy. Some persons tend to minimize or even deny symptoms. There may be a skin lesion that goes unnoticed, or a change in bowel habits that goes unreported. Or there may be emotional, social, sexual, or alcohol problems that will remain unrevealed unless questions are specifically directed to the problems.

Probably no part of the checkup is more important than the history of the patients' account of his health status as reported to the physician. So much can be made of just what the patient complains of, how he describes these complaints, what he views as their meaning, and finally what he elects to leave out. Many physicians believe that, if left to a single approach to the patient, the careful taking of a history should be given preference over everything else. It is remarkable how often the history alone leads to a diagnosis. This feature of the examination must remain the responsibility of the physician, though he may be aided but not substituted by non-physician personnel, multiphasic screening or perhaps ultimately even computers.

The principal questions that need to be answered with respect to periodic health examinations are (1) should everyone have one (2) how often and (3) how complete?

Periodic health examinations in middle age and beyond are intended principally to prevent death from cancer (cf chapter on cancer), to discover other diseases in their early and curable state, and to delay the onset and slow the progress of cardiovascular and cerebrovascular disease. This means essentially diagnosing cancer and other diseases when they are still curable, and eliminating risk factors in atherosclerotic disease, namely hypertension, hypercholesterolemia, cigarette smoking and perhaps obesity and physical inactivity. Much of this can be and is being accomplished by health education through the public media.

In the apparently healthy person who appears in the physician's office for a "physical" the unique role of the physician is (a) to use the force of his authority and personality to persuade the patient to follow sensible health measures and (b) to screen for illness that is treatable. Some of the illnesses that are treatable such as hypertension are, as previously indicated, easily discovered on physical examination; some, such as anemia, on a simple laboratory examination. Thereafter, the person, no longer normal, becomes a patient to be treated. But the treatment is for the recognized disorder, apart from which the patient is presumably normal. And for the normal aspects that the patient presents, the difficult questions mentioned above remain: how much should be done with respect to other than the illness under treatment, and how often in order to discover what?

An attempt to answer these questions is made by Breslow and Somers who note that "...it is impossible at present to list for this age group (40-59 years)

preventive procedures that would receive universal professional approval. The spectrum of opinion still varies from those who hold firmly to the need for a complete annual checkup to those who claim that nearly all preventive services are wasted."³ Breslow and Somers suggest one complete professional examination at 40 and subsequent screening at 2-3 year intervals for obesity, complications from smoking, hypertension, and cancer. At five year intervals they recommend screening for alcoholism, anemia, diabetes, vision and hearing defects, and for the high risk groups, tuberculosis and syphilis.

Note particularly, the absence of x-ray examination of the lungs, and tonometry as routine screening procedures. Except for heavy smokers and other high-risk groups, the routine chest x-ray study in the view of many can no longer be justified at this age. Indeed, there are those who question its value even in high risk groups (cf chapter on cancer). For glaucoma, both the reliability of the existing screening procedures and the value of treatment before the onset of visual field loss are now being questioned.

Among other tests whose routine application is professionally questioned by some are those for diabetes. It is not clear that there is any value in detecting diabetes in the age group (above 40) until symptoms appear.³

Criteria for Disease Screening

Since "...we do not have the means, tradition or system for rationally examining in desirable detail everything that is done or proposed in medicine...it will be necessary to make some decisions on the basis of 'prudent' evaluation of what evidence exists."³ Frame and Carlson⁴ have made just such an attempt in an article in which they list certain general criteria that they believe justify screening for particular diseases. These criteria seem reasonable and are as follows:

1. The disease must have a significant effect on quality or quantity of life.
2. Acceptable methods of treatment must be available.
3. The disease must have an asymptomatic period during which detection and treatment significantly reduce morbidity and/or mortality.
4. Treatment in the asymptomatic phase must yield a therapeutic result superior to that obtained by delaying treatment until symptoms appear.
5. Tests must be available at reasonable cost to detect the condition in the asymptomatic period.
6. The incidence of the condition must be sufficient to justify the cost of screening.

For the time being it must be left to the physician to decide what is "sound and practical" that is, what the physician and the patient are comfortable with. It is in this respect that factors such as reassurance, intellectual satisfaction, and considerations of malpractice appear as modifying factors.

Current Recommendations

In the light of current knowledge I should consider

Continued on Page 54

...in the functional bowel/irritable bowel syndrome*

Bentyl[®]

(dicyclomine hydrochloride USP)

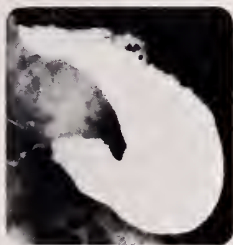
10 mg. capsules, 20 mg. tablets,
10 mg./5 ml. syrup, 10 mg./ml. injection

helps control abnormal motor activity
with minimal anticholinergic side effects†

Demonstrated smooth muscle relaxant activity.

In this double-blind study, twenty patients having G.I. series and exhibiting spasm were randomly selected to receive either 2 cc. of Bentyl or sodium chloride intramuscularly. Ten minutes after the injection another radiograph was taken . . .

. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.



Pylorospasm has almost totally blocked passage of barium meal.



Barium meal beginning to pass 10 minutes after intramuscular injection of 20 mg. Bentyl.

“The correlation of spasm relief and drug given was excellent.”

*This drug has been classified “probably” effective in treating functional bowel/irritable bowel syndrome.

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:

King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964.

Merrell

8-4420 (Y736A) MNR-804

Bentyl®

(dicyclomine hydrochloride USP)

Capsules, Tablets, Syrup, Injection

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Brief Summary

INDICATIONS

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the following indications as "probably" effective

For the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

THESE FUNCTIONAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS.

For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS: Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloro-duodenal stenosis), paralytic ileus, intestinal atony of the elderly or debilitated patient, unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis, toxic megacolon complicating ulcerative colitis, myasthenia gravis. **WARNINGS:** In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. **PRECAUTIONS:** Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with Autonomic neuropathy. Hepatic or renal disease. Ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur. **ADVERSE REACTIONS:** Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia; urinary hesitancy and retention; blurred vision and tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste, headache, nervousness; drowsiness, weakness, dizziness; insomnia, nausea, vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis, urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. **DOSEAGE AND ADMINISTRATION:** Dosage must be adjusted to individual patient's needs.

Usual Dosage: Bentyl 10 mg capsule and syrup: Adults: 1 or 2 capsules or teaspoonfuls syrup three or four times daily. Children: 1 capsule or teaspoonful syrup three or four times daily. Infants: ½ teaspoonful syrup three or four times daily. (May be diluted with equal volume of water.) Bentyl 20 mg: Adults: 1 tablet three or four times daily. Bentyl Injection: Adults: 2 ml (20 mg) every four to six hours intramuscularly only. NOT FOR INTRAVENOUS USE. **MANAGEMENT OF OVERDOSE:** The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine® (bethanecol chloride USP) should be used.

Product Information as of October, 1978.

Injectable dosage forms manufactured by CONNAUGHT LABORATORIES, INC., Swiftwater, Pennsylvania 18370 or TAYLOR PHARMACAL COMPANY, Ocatator, Illinois 62525 for MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc., Cincinnati, Ohio 45215, U.S.A.

as reasonable the following: For persons aged 20-40, checkups every five years to include the customary history and physical examination, and the following tests: Hct., WBC, and BSR, urinalysis, serum cholesterol, (preferably lipoprotein electrophoresis for HDL, LDL, and VLDL) uric acid and blood sugar. Also tonometry, stool for occult blood x3, Pap smear annually for 5 years and if negative every 3 years, and an initial chest x-ray and electrocardiogram.

For persons aged 40-65, checkups every two years, with again an initial chest x-ray and electrocardiogram; and from 65 on, the same again, but on an annual basis. The electrocardiogram and chest x-rays are therefore done at ages 20, 40, and 65. Otherwise they are done only when specifically indicated. For women who are at high risk for breast cancer, yearly mammograms are recommended after age 40; for those not at risk, every two years after age 55.

Automated biochemical screening is now in wide use. Its overall value, like that of the periodic health examination itself, is regarded by some as not medically justified. For while the biochemical screening produces a great deal of laboratory data at small unit cost to the patient, its cost to the total patient population is considerable. Hence, its cost effectiveness (bearing in mind the problem of false-positive results and unnecessary treatments) is questioned.⁵ However, for a number of reasons including the reassuring benefit of normal findings, there are those who see the automated biochemical profile as economically justifiable.⁶ As a matter of fact it is now established practice.

I know of no helpful data to indicate how often asymptomatic patients over 70 or 75 years of age should be examined. Many such patients are seen at frequent intervals anyway for the care of chronic illnesses. It is possible that no more than this is needed beyond the care of new symptoms as they arise.

This approach is, to be sure, arbitrary and tentative; hence must remain flexible. Cautious practical wisdom on the part of physicians, who have the benefit of personal observation of each patient to guide them, provides the basis for the best course to follow.

FINAL COMMENT

There remains the question of regulations that may be imposed which might greatly modify all of the previous discussion. Already, there has been discussion in Congress with suggestions that medical insurers set limits on how much may be spent on testing.

In view of the understandable concern over the sharply rising and largely uncontrolled costs of health care, we may anticipate increasingly aggressive cost-control efforts. These will probably create competitive mechanisms that provide in some manner rewards for those who cut costs and penalties for those who don't. The measures will be instituted either by the government through more or less arbitrary regulations or private insurance carriers

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CONTINUING MEDICAL EDUCATION IN MAINE

Conferences and Workshops

Title: Diabetes Update
Date: March 29, 1980
Location: A.R. Gould Memorial Hospital, Presque Isle
Sponsors: Aroostook County Regional Medical Standards Committee (PSRO); A.R. Gould Memorial Hospital, and Medical Care Development
Credit: AMA Category I—6 hours
Reg. Fee: To be determined
For further information contact Gerald Goold, Medical Care Development; 622-7566.

Hospital Activities Augusta General Hospital Augusta, Maine

Feb. 26, 1980 **A Microbiologic Approach to Infections in the Abdomen**
7:30-8:30 a.m. David R. Ginder, M.D., Mid-Maine Medical Center

March 25, 1980 **Pulmonary Disease**
7:30-8:30 a.m. Peter Barlow, M.D., Dartmouth Medical School
These programs have been certified AMA Category I and AAFP (prescribed). For further information contact Mrs. Nancy Favorite; 623-4711. These programs may be viewed over ITS.

Augusta Mental Health Institute Augusta, Maine

Feb. 14, 1980 **Psychotherapy of Schizophrenic**
10-11:30 a.m. Edward Messner, M.D., Harvard Medical School Faculty, Massachusetts General Hospital

1:30-3 p.m. **The Psychotherapeutic Alliance**
Psychotherapeutic Program

March 6, 1980 **Factitious Illness**
10-11:30 a.m. Theodore Stern, M.D., Harvard Medical School Faculty, Massachusetts General Hospital

1:30-3 p.m. **Headache and the Diagnosis of Tumor**
Medical Unit

These sessions are Grand Rounds. All programs have been certified AMA Category I. For further information contact Pauline H. Soper; 622-3751.

Eastern Maine Medical Center Bangor, Maine

Every Mon.	EEG Conference	12-1 p.m.
Every Mon.	Surgical Service—Chief's Rounds	5-6 p.m.
4th Mon.	ENT Section Meeting	12-1 p.m.
4th Mon.	Neurosurgery Section Meetings	4-5 p.m.
3rd Tues.	Dermatology-Pathology Conference	5-6 p.m.
3rd Tues.	Dermatology Section Meeting	6-7 p.m.
4th Tues.	Pulmonary Medicine Section Meeting	8-9 a.m.

1st Wed.	Hematology/Oncology Meeting	8-9 a.m.
Every Wed.	Tumor Clinic Conference	2-5 p.m.
Every Wed.	Radiology Conference	5-6 p.m.
	(1) Ultrasound/Nuclear Medicine	
	(2) Radiology Film Review	
	(3) Neuroradiology	
	(4) Teaching File Conference	
	(5) G.I. Radiology	
1st Thurs.	Ophthalmology Section Meeting	7:30-8:30 a.m.
	OB-GYN Conference	8-9 a.m.
	(1) Pathology	
	(2) GYN Analysis	
	(3) OB-Pediatric Combined	
	(4) In-Service and Education	
Every Thurs.	Pediatric Grand Rounds	9-10 a.m.
Every Thurs.	Medical Service Conference	10-11 a.m.
Every Thurs.	Cardiology Conference	11 a.m.-1 p.m.
2nd Thurs.	Orthopedic Grand Rounds	7:45-8:45 a.m.
4th Thurs.	Orthopedic Service Meeting	7:30-9 a.m.
4th Thurs.	Surgical Service Death Review	7:45-8:45 a.m.
Every Thurs.	Psychiatric Service Grand Rounds	10-11 a.m.
4th Thurs.	Urology Section Conference	7:30-8:30 a.m.
Every Fri.	Neurology Grand Rounds	8-9 a.m.

Visiting Professor Program:

2nd Thurs.	Medical Service Visiting Professor	10 a.m.-5 p.m.
2nd Thurs.	Anesthesia Service Visiting Professor	7-8 a.m.
3rd Thurs.	OB/GYN Service Visiting Professor	10 a.m.-4 p.m.
Saturdays	Surgery Service Visiting Professor	8 a.m.-Noon
4th Thurs.	Pediatric Service Visiting Professor	10 a.m.-5 p.m.
as scheduled	Orthopedic Service Visiting Professor	
as scheduled	Family Practice Visiting Professor	
as scheduled	Psychiatric Service Visiting Professor	
as scheduled	Radiology Service Visiting Professor	

All activities have been certified AMA Category I. For further information contact James F. Lawsing, III, M.D., Coordinator, Medical Education; 947-3711 Ext. 330.

Henrietta D. Goodall Hospital Sanford, Maine

Feb. 26, 1980 **What's New in Endocrinology**
David Slovick, M.D., Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

March 18, 1980 **Office GYN**
Elliot Rivo, M.D., Newton-Wellesley Hospital, Harvard Medical School, Newton Lower Falls, Massachusetts

These meetings will be held at the Henrietta D. Goodall Hospital's Conference Room at 7 p.m. These programs have been certified AMA Category I and AAFP (prescribed). For further information contact Melvin Bacon, M.D.; 324-3632.

**A. R. Gould Memorial Hospital
Presque Isle, Maine**

March 17, 1980 **Infertility and Fertility Control**
Douglas Marchant, M.D., Tufts University
School of Medicine

Every Mon. Grand Rounds. Topics and speakers to be
7:30 p.m. announced

These meetings will be held at the Rotary Regional Educational Center
at the A. R. Gould Memorial Hospital. These programs have been cer-
tified AMA Category I. For further information contact Marilyn Dean;
769-2511.

**Maine Medical Center
Portland, Maine**

Every Mon.	Student Technologist Conference	8 a.m.
Every Mon.	Hematology-Pathology Conference	11 a.m.
Every Mon.	Pulmonary Conference	12 Noon
Every Mon.	Pediatric Residents' Conference	1 p.m.
Every Mon.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Mon.	Surgical Pathology Review	4 p.m.
Every Mon.	Radiology Journal Club	5 p.m.
1st &	Clinical Nephrology Conference	11 a.m.
3rd Mon.		
1st &	Hematology-Pathology Conference	12 Noon
3rd Mon.		
3rd Mon.	Eye Conference	11:45 a.m.
Every Tues.	Radiology Residents' Seminar	7 a.m.
Every Tues.	Family Practice Grand Rounds	9 a.m.
Every Tues.	Electrocardiographic Interpretation	1 p.m.
Every Tues.	Psychiatric Grand Rounds	1:30 p.m.
Every Tues.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Tues.	Surgical Seminar	4 p.m.
Every Tues.	Pathology Slide Seminar	4 p.m.
1st &	Radiology-Pathology Conference	12 Noon
3rd Tues.		
1st &	Neurology Conference	12 Noon
4th Tues.		
2nd Tues.	Infectious Disease Conference	12 Noon
3rd Tues.	Hematology Conference	12 Noon
5th Tues.	Oncology Conference	12 Noon
Every Wed.	Radiation Therapy Conference	7 a.m.
Every Wed.	Urology Conference	7 a.m.
Every Wed.	Student Technologist Conference	8 a.m.
Every Wed.	Continuing Education Seminar	8 a.m.
Every Wed.	Medical Conference	9 a.m.
Every Wed.	Psychiatric Journal Club	12 Noon
Every Wed.	Cardiology Seminar	12 Noon
Every Wed.	Surgical Grand Rounds	5 p.m.
2nd Wed.	Guest Internist—Medical Conference	9 a.m.
4th Wed.	Medical Mortality Conference	9 a.m.
Alt. Wed.	Neurology-Psychiatry Seminar	11 a.m.
Alt. Wed.	Anesthesiology Journal Club	3 p.m.
Every Thurs.	Thoracic Surgery Conference	7 a.m.
Every Thurs.	OB/GYN Conference	7 a.m.
Every Thurs.	Anesthesiology Clinical Conference	7 a.m.
Every Thurs.	Diagnostic Radiology Teaching Conference	7 a.m.
Every Thurs.	Surgical Conference	8 a.m.
Every Thurs.	Pediatric Conference	9 a.m.
Every Thurs.	Tumor Consultation Board	11 a.m.
Every Thurs.	Medical Residents' Conference	12 Noon
Every Thurs.	Surgical Seminar	4 p.m.
Every Thurs.	Endocrinology Conference	5 p.m.
Every Thurs.	Dental Specialty Lecture	6 p.m.

1st Thurs.	Anesthesia Mortality Conference	7 a.m.
1st Thurs.	Guest Pediatrician	9 a.m.
1st Thurs.	Gastroenterology Conference	12 Noon
1st &	Cardiac-Surgical Conference	12:30 p.m.
3rd Thurs.		
1st, 3rd, &	Pulmonary-Physiology Conference	12:30 p.m.
5th Thurs.		
2nd Thurs.	Cardiology Teaching Conference	12:30 p.m.
2nd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
2nd Thurs.	Eye Staff Scientific Session	5:30 p.m.
2nd Thurs.	Maine Medical Center Medical Staff Meeting and Scientific Session	6 p.m.
2nd &	Pulmonary-Pathology Conference	12 Noon
4th Thurs.		
2nd &	Endocrinology Conference	12 Noon
4th Thurs.		
3rd Thurs.	Combined Guest Physician or Guest Surgeon Program	8 a.m.
3rd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
4th Thurs.	Surgical Mortality Conference	8 a.m.
4th Thurs.	Anesthesia Mortality Conference	3:30 p.m.
Last Thurs.	Pediatric Mortality Conference	9 a.m.
Every Fri.	Thoracic-Surgical Conference	7 a.m.
Every Fri.	Nuclear Medicine Conference	7 a.m.
Every Fri.	Student Technologist Conference	8 a.m.
Every Fri.	Neurological-Neurosurgical Conference	8:30 a.m.
Every Fri.	Gastroenterology Conference	9 a.m.
Every Fri.	Medical Rehabilitation Staff Conf.	9 a.m.
Every Fri.	Orthopedic Conference	9 a.m.
1st Fri.	Dermatology Conference	12 Noon
2nd Fri.	Nephrology Conference	12 Noon
3rd Fri.	Rheumatology Conference	12 Noon
4th Fri.	Oncology Conference	12 Noon
Alt. Fri.	Oncology Radiation Conference	7 a.m.
Alt. Fri.	Gastroenterology Conference	10 a.m.

All programs have been certified AMA Category I. For further informa-
tion contact Costas T. Lambrew, M.D.; 871-2111.

**Mercy Hospital
Portland, Maine**

March 6, 1980 **Stress Hypertension and Therapy**
7 p.m. Ray Rosenman, M.D., Head of Cardiac
Research Program, Mt. Zion Hospital, San
Francisco, California

This program will be held in the Mercy Hospital auditorium and has
been certified AMA Category I. For further information contact Gwen
Gray; 774-1461.

**Mid-Maine Medical Center
Waterville, Maine**

Feb. 21, 1980 **Q Fever**
David R. Ginder, M.D., Mid-Maine Medical
Center

Feb. 28, 1980 **Nephrotoxicity of Common Therapeutic Agents**
John Engle, M.D., Mid-Maine Medical Center

March 6, 1980 **Pulmonary Infections in Immunosuppressed
Patients**
James Pennington, M.D., Peter Bent Brigham
Hospital, Boston, Massachusetts

March 13, 1980 **Psychiatric Liaison Issues**

Continued on Page 57

Robert Crowell, M.D., Mid-Maine Medical Center

March 20, 1980 **Cancer Chemotherapy—Oat Cell Carcinoma and Melanoma**
Larry Nathanson, M.D., Tufts University School of Medicine, Boston, Massachusetts

March 27, 1980 **Case Presentation**
Family Practice Residents

All programs are being held at Mid-Maine Medical Center in the South Wing Conference Room from 12-1 p.m. and have been certified AMA Category I and AAFP (elective). These programs may be viewed over ITS. For further information contact David R. Ginder, M.D.; 873-0621.

Penobscot Bay Medical Center Rockland, Maine

March 14, 1980 **Medical Ethics**
11 a.m. Jennifer Daley, M.D., Assistant Professor of Medicine, Tufts University School of Medicine

This program, which will take place at the conference room of the Penobscot Bay Physicians Building, has been certified for two hours of AMA Category I credit. For further information contact Lloyd Roberts, M.D., 594-9511, ext. 151.

March 18, 1980 **Tumor Conference**
12 p.m.
Program has been certified for one hour of AMA Category I credit. For further information contact Stephen A. Ross, M.D., 594-9511.

V. A. Hospital Togus, Maine

General Staff Meetings

March 3, 1980 **Nuclear Medicine**
2 p.m. Oncology Service

March 11, 1980 **Peripheral Vascular Surgery**
12 Noon Ferris S. Ray, M.D., Maine Medical Center (ITS Presentation)

March 17, 1980 **Rehabilitation Medicine Service**
2 p.m.

March 21, 1980 **Neurobehavior**
11 a.m. Michael Alexander, M.D., Director, Behavioral Unit, Boston VA Hospital (ITS Presentation)

March 31, 1980 **Laboratory Service**
2 p.m.

Medical Service Staff Meetings

Every Wed. 1:15 p.m. Staff Meeting. Topics to be announced.

2nd Wed. 1:15 p.m. Review of Records

Every other Thurs. Oncology Clinic

These programs have been certified AMA Category I. For further information contact E. Osborne Coates, Jr., M.D.; 623-8411.

ANNOUNCEMENT: Medical Care Development, Inc. is now receiving a listing of continuing medical education activities taking place in Vermont, New Hampshire, and Massachusetts. If you wish further in-

Maine Society for the History of Medicine

The third meeting of the Maine Society for the History of Medicine will meet on Saturday, March 29, 1980 at 2:00 p.m. at the Augusta Mental Health Institute (Greenlaw Auditorium).

Earl Shettleworth, Director of the State Historic Preservation Commission, will speak on the subject of Historic Medical Buildings of Maine.

A brief tour of historically relevant parts of A.M.H.I. will be followed by dinner at Hazel Green's.

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Spring Meeting of the M.M.A. House of Delegates

Saturday, March 22, 1980

Mid-Maine Medical Center (Thayer Unit), Waterville, Maine

12:30 P.M.—Registration; 1:00 P.M.—Lunch; 2:00 P.M.—Meeting

9:30 A.M.—Meeting of the Executive Committee

the Medicaid Fraud Control Unit, was then presented to the Society after introductory comments by Dr. Andrews. Mr. Seaberg summarized the work of the Medicaid Fraud Control Unit. A lively question and answer period followed this. A great deal of interest was evidenced by Dr. Sidney Block who sought guidance in billing procedures for his office.

The Resolutions Committee was then called upon to present a resolution on Dr. Rudolf Eyerer. Dr. Dexter Clough read a resolution offered by Dr. John Kaiser. This was accepted by the membership and will be made a permanent part of the record. In addition to this, a copy of the resolution will be forwarded to Dr. Eyerer's family.

Since there was no further business to take care of, the meeting was adjourned shortly after 9:00 p.m.

JAMES R. CURTIS, M.D., *Secretary*

Somerset

The regular meeting of the Somerset County Medical Society was held at Shirley's Diner in Skowhegan on October 16, 1979. There were 19 members present and their wives.

A letter from the Assistant District Attorney was read to the members. It was about the Medicaid Fraud Control Unit.

A special assessment fee was voted for the year and an increase in the annual dues was voted after reporting the year's budget to the members.

The letter of Dr. Melvin Bacon, Chairman of the Diabetes Detection Committee, was also read to the members.

Election of officers also took place at this meeting:

President: Dr. John H. Steeves, Skowhegan

Vice-President: Dr. Iver Nielson, Skowhegan

Delegate to the M.M.A. House of Delegates: Dr. Robert Steinhacker, Skowhegan. Alternate: Dr. Lester K. Henderson, Jr., Skowhegan

Representative of the 5th District to the Executive Committee of the M.M.A.: Dr. Richard C. Taylor, Skowhegan

The meeting was adjourned at 6:45 p.m.

VINCENTE L. SY, M.D., *Secretary*

Kennebec

The Kennebec County Medical Association met at the John Martin's Manor Restaurant in Waterville on October 18, 1979. Following a pleasant cocktail hour and baked chicken dinner, Dr. Towne called the meeting to order. Dr. Feagin read a letter from the Maine Heart Association regarding a blood pressure screening program to be conducted in conjunction with the Laverdiere's chain of drug stores. Members of the Association expressed some lack of willingness to cooperate with this particular program and that will be communicated.

The applications of Drs. John E. Macklin, Peter F. Jeffries and Jeanne F. Arnold were voted on and were unanimously elected to membership in the Association. Dr. Towne then introduced Mr. Milton Huntington of the Maine Petroleum Association who discussed the current petroleum and oil shortage and handled a rather interesting series of questions from the members with some degree of calm.

The meeting was adjourned at 9:00 p.m.

The Kennebec County Medical Association met at the Guido Wine Cellar in Augusta on November 15, 1979. Following the usual cocktail hour and a pleasant roast beef dinner, Dr. Towne called the meeting to order.

There was correspondence regarding the hearing on Regulations concerning CME. Dr. Feagin discussed a little bit the deliberations of the Executive Committee concerning the negotiations with Blue Shield and urged the delegates to the House of Delegates to please attend the meeting on Saturday.

Dr. Towne then introduced Dr. Leo Cousineau of Lewiston who presented a very insightful discussion of the development of the National Health Insurance System in Canada and reactions of some of the physicians there including his own, and described why he left and came to the States.

The meeting adjourned at 9:30 p.m.

O. THOMAS FEAGIN, M.D., *Secretary*

Aroostook

A regular meeting of the Aroostook County Medical Society was held at the Northeastland Hotel in Presque Isle on October 24, 1979. Nineteen active members were in attendance. The business meeting was preceded by two speakers: Mr. Guy Seaberg, Assistant Attorney General, spoke about the Medicaid Fraud Control Unit recently set up in Augusta to combat problems of fraud among Medicaid providers. Dr. Brinton T. Darlington, President of the Maine Medical Association, addressed the reasons for the increase in M.M.A. dues for 1980.

The business meeting was called to order by the President, Dr. Rodrigue J. Albert. Because of the lateness of the hour, it was voted to dispense with the reading of the minutes of the previous meeting. Copies of the minutes were handed out.

An application for membership was received from Dr. Donald Noble of Fort Kent, dated Aug. 2, 1979. The application had been reviewed and accepted by the Credentials Committee. It was unanimously voted to accept Dr. Noble as a member.

The Maine Affiliate of the American Heart Association, in cooperation with Laverdiere's Drugstores, will be holding Hypertension Screening Clinics at each Laverdiere's store in November, January, or February. The detection and referral criteria that they will use are on file.

Senator William Cohen responded to an invitation to address the Society on the concept of National Health. A date has not yet been set for his talk.

Dr. Melvin Bacon, Chairman of the Diabetes Committee of the M.M.A., sent a lengthy report on his plans to set up an extensive Diabetes Detection and Education Program in Maine.

Dr. Philip Gibbs will become an affiliate member. He is at present in a two-year fellowship at the University of Washington.

A letter was received from John Bielecki, recipient of a \$500 scholarship in 1978, asking that he be considered again this year for scholarship help. It was decided to table his request until next year as the 1979 scholarship has already been awarded.

Dr. Craig W. Young gave a report on the Health Care Financing Committee of the M.M.A. in which he talked at length on the M.M.A.'s current negotiations for a new contract with Blue Shield of Maine. He also gave a report on the Executive Committee of the M.M.A., stating that the primary goal of the Executive Committee for 1980 is to review twelve standing committees to ascertain if they are carrying out their intended function. Dr. Young made a plea for more committee participation among Society members.

The next annual meeting of the M.M.A. will be held at The Balsams, Dixville Notch, New Hampshire.

It was voted to increase Society dues to \$50 in 1980. These will be collected by the secretary of the M.M.A. State dues for 1980 will be \$325.

Dr. Alroy Chow suggested that the Society invite Mr. Grant Heggie to speak at our next meeting. Mr. Heggie is Vice-President of the Maine Hospital Association and has coordinated the recent efforts of the seven area hospitals to develop long range planning for the area.

Dr. Donald G. Brushett stated that he received a letter from ACAP's Chairman, Dana Connors, in response to a meeting between ACAP's Executive Committee and a group of physicians, representing the Society and opposed to ACAP's Family Planning Program. Mr. Connors stated that the Executive Committee felt the need still exists for family planning services in Aroostook County and that the quality of care delivered at ACAP Family Planning Clinics is excellent.

No further business to be discussed, the meeting was adjourned.

JANET M. PARKER, M.D., *Secretary*

Knox

The Knox County Medical Society met at the Sail Loft Restaurant in Rockport on November 6, 1979, at 6:30 p.m., with seventeen members in attendance. Following the dinner, a short

business meeting was held. This time a nominating committee consisting of Drs. John Wickenden, John Williams and Corwin Olds was appointed. They are charged with producing a slate of officers for next year and the replacement for Dr. John Wickenden's position on the Executive Committee whose term ends June 1980. Additionally, at the request of the secretary, the Society nominated a member to fill Dr. Wickenden's remaining term on the Executive Committee of the Maine Medical Association. This representative will be Dr. Albert Lantinen, Jr. Additionally, a letter from Dr. David Reed was read indicating his change in status because of a current move in his position as a delegate to the Maine Medical Association will be nominated by the next meeting.

Following the business meeting, an excellent presentation of the Hospice Concept and Mid-Coast Family Hospice Movement was given by Mr. Val Gauge and Ms. Brenda Hart. This prompted lively discussion involving Hospice Concept and the use of ancillary agencies for the care of all patients.

ALBERT J. LANTINEN, JR., M.D., *Secretary*

Washington

A regular meeting of the Washington County Medical Society was held on October 29, 1979 at the Peavey Memorial Library, Eastport, with the meeting opened at 7:30 p.m. under the direction of Dr. James C. Bates, President of the Medical Society.

I. Minutes of the last meeting, read and approved.

II. The proposal that was made at an earlier meeting of the

Washington County Medical Society, that each County have a Delegate to the Executive Board, has been passed.

III. Discussion of Medicare billing, which was brought up, also at a prior meeting was discussed, as well as billing for the State Medicaid cases.

IV. It was brought to the attention of the members of the Society of the new address of the Maine Medical Association: 524 Western Ave., Augusta, Maine 04330, with Frank O. Stred, Executive Director.

V. It was also brought up, the question of increased dues, beginning Jan. 1, 1980.

VI. Members also advised that the next meeting of the Maine Medical Association will be at The Balsams, Dixville Notch, New Hampshire.

VII. Diabetes Month, November, was brought up for discussion with a letter from Dr. Melvin Bacon, Chairman for the State, which was passed around with general information.

VIII. There was some discussion of what the Maine Health Information Center was to accomplish.

IX. Members wishing to be on any Standing Committee, or other committees, were asked to submit their names.

X. Members asked about the feelings about Blue Cross/Blue Shield Group Insurance. They all felt that they would favor staying with Blue Cross/Blue Shield at the present time.

XI. The next meeting to be January 21, 1980, at the Down East Community Hospital, Machias, in the Medical Library Room.

KARL V. LARSON, M.D., *Secretary*

HERNIATED INTERVERTEBRAL DISC: An Outline of the Current Diagnosis and Management

Continued from Page 42

area is more common, but is not affected by the type of surgery performed. In my experience, there is no difference in the percentage of recurrence when attempt is made at emptying the interspace than when only the herniated fragment is removed without disturbing the remainder of the disc. The results of this type of surgery are excellent and in my experience are better than when more extensive surgery is carried out.

The poor results of surgery are usually secondary

to mistaken diagnosis and other factors as the patient's inadequate personality or secondary gains in compensation cases.

In summary, the diagnosis of a nerve root compression syndrome secondary to a herniated disc fragment should be easily recognized by the average practitioner and handled adequately.

The result of surgery in my own practice has been excellent when the presently outlined criteria has been followed.

FINE NEEDLE ASPIRATION BREAST BIOPSY: A Six-Year Experience With 1034 Aspirations

Continued from Page 49

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DIAGNOSTIC IMPERATIVES IN INTERNAL MEDICINE—Continued from Page 54

through the support of strong utilization—control programs. Such programs could stimulate the development of a variety of competitive prepaid health plans, all of which are likely to be followed by more imposed regulations.

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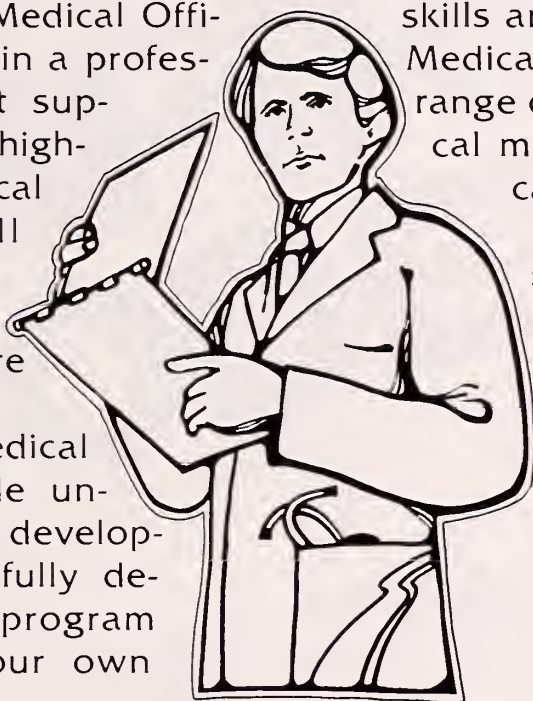
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BRINTON T. DARLINGTON, M.D., Augusta	Alternate Delegate to the AMA	Dec. 31, 1981
HARRY A. BLISS, M.D., Portland	Ex-Officio	1980

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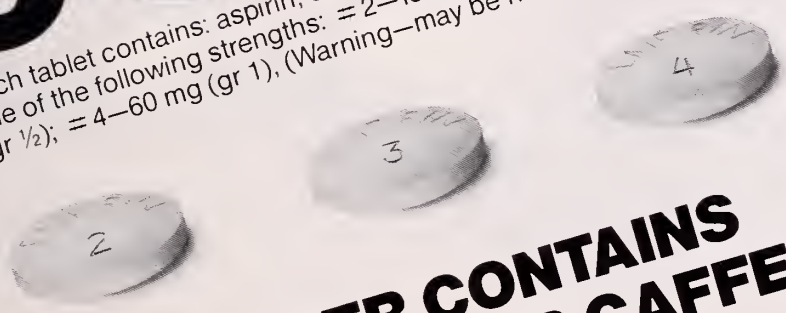
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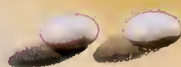
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Brief Summary

INDICATION

Nausea and vomiting of pregnancy.

PRECAUTIONS

Because of potential drowsiness, Bendectin should be prescribed with caution for patients who must drive automobiles or operate machinery.

Studies in rats and rabbits have revealed no suggestion of drug-induced fetal abnormalities at doses of Bendectin up to 90 times the maximum human dose. In addition, several epidemiologic studies in women who received Bendectin during pregnancy have shown that the incidence of birth defects in their offspring is no higher than in women not taking the drug during pregnancy. Nevertheless, like all drugs considered for use during pregnancy, particularly during the first trimester, Bendectin should be used only when clearly needed.

ADVERSE REACTIONS

The adverse reactions that may occur are those of the individual ingredients. Doxylamine succinate may cause drowsiness, vertigo, nervousness, epigastric pain, headache, palpitation, diarrhea, disorientation, or irritability.

Pyridoxine hydrochloride is a vitamin that is generally recognized as having no adverse effects.

DOSAGE AND ADMINISTRATION

2 Bendectin tablets at bedtime. In severe cases or when nausea occurs during the day: 1 additional Bendectin tablet in the morning and another in midafternoon.

Product Information as of January, 1978

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Number 3

Premature Biopsy of a Neck Mass: Otolaryngologic Considerations

BENJAMIN F. LOUNSBURY, M.D.*

INTRODUCTION

One of the saddest situations a head and neck surgeon encounters is a patient whose prognosis for survival has been significantly impaired by a premature or inappropriate biopsy of a neck mass. Virtually all practitioners encounter patients with cervical lymphadenopathy or a "lump in the neck." This article is intended to help the physician who lacks experience in managing head and neck cancer not to make a serious management error. It will briefly describe the anatomy, physiology, and pathology of the cervical lymph nodes, as well as surgical problems specific to the area. Finally, it will provide a reasonable guideline for management of enlarged cervical lymph nodes and neck masses.

ANATOMY AND PHYSIOLOGY

The neck contains large numbers of lymph nodes. Radical neck dissection specimens routinely contain more than fifty nodes on one side. The nodes are arranged in a fairly consistent pattern. A numbering system has been agreed upon by surgeons working with head and neck cancer patients to allow consistent reporting of nodal metastasis. Ten areas are designated by this system. Areas 1 through 4 are located along the sternocleidomastoid muscle, with area 1 being the highest and 4 the lowest. Areas 5 and 6 are in the "posterior triangle," the space bordered superiorly by the sternocleidomastoid and the trapezius muscles and inferiorly by the clavicle. Areas 7 through 10 are less frequently involved and are all anterior to the sternocleidomastoid. Each of these areas receives afferent lymph vessels from specific regions in the head and neck. With knowledge of the drainage patterns of the head and neck, a practitioner can make an educated guess concerning the location of a pathologic process causing lymph-

adenopathy. When more than one area is involved (multiple nodes or one very large node), the accuracy of prediction understandably worsens. Generally, lymph flows down in the neck, but in the presence of pathology, retrograde flow of lymph, infective bacteria, or metastatic cells is common. Therefore, the highest enlarged node where many are present has no particular importance.

A list of the areas of the neck and organs which most frequently give rise to metastases in those areas is provided.¹

1. Superior Jugular (nodes within the tail of the parotid gland)
 - a. Nasopharynx
 - b. Base of Tongue
 - c. Palatine Tonsil
 - d. Parotid Gland
 - e. Larynx
2. Upper Middle Jugular (tonsil nodes, subdiaphragmatic nodes)
 - a. Palatine tonsil
 - b. Tongue and other oral structures
 - c. Larynx
 - d. Oropharynx and hypopharynx
 - e. Paranasal sinuses
3. Lower Middle Jugular
 - a. Larynx
 - b. Cervical esophagus
 - c. Hypopharynx
 - d. Thyroid
4. Inferior Jugular
 - a. Thyroid
 - b. Larynx
 - c. Cervical esophagus
5. Spinal Accessory
 - a. Nasopharynx
 - b. Thyroid
6. Supraclavicular
 - a. Lung

*Central Maine Medical Center, Lewiston, Maine 04240.

- b. Breast
- c. Any head and neck primary
- d. Other primaries below the clavicle (stomach, ovary, prostate, colon and rectum, pancreas, biliary, uterus, liver, kidney, in approximately that order).²
- 7. Submandibular
 - a. Intra-oral primary
 - b. Submandibular salivary gland
- 8. Submental
 - a. Lip
 - b. Anterior floor of mouth and alveolar ridge
 - c. Buccal wall
- 9. Cricothyroid (delphian)
 - a. Larynx
 - b. Thyroid
- 10. Pre-auricular
 - a. Parotid gland
 - b. External ear canal
 - c. Skin of lateral face, temporal region, and scalp.

PATHOLOGY

There are three basic processes that can cause enlargement of cervical lymph nodes. First, and most common in children, is inflammation in a head and neck site or in the nodes themselves. We are all familiar with the enlargement of the nodes at the angles of the jaws that invariably accompanies tonsillitis or pharyngitis, and the enlargement of the nodes along the spinal accessory chain that frequently accompanies adenoiditis. Second is cancer metastatic to the nodes from local or distant sites. In adults, nodal metastasis from squamous cell carcinoma in a head or neck site is the cause of the mass in over 50 percent of patients who consult a physician because of a lump or a mass in the neck. Many of these patients have other "less disturbing" symptoms such as a sore in the mouth or hoarseness, but some of them have no symptoms suggestive of a malignancy. Common sites for "silent primaries" are the nasopharynx, base of tongue and hypopharynx. The third process is malignancy intrinsic to the nodes themselves, such as lymphoma.

THERAPY

Most infectious processes respond to appropriate antibiotic therapy with or without incision and drainage. Frequently, the shrinkage or disappearance of a lymph node after antibiotic therapy is taken as evidence that an infectious process caused its enlargement in the first place. Occasionally a node itself becomes necrotic, the locus of an abscess.

Squamous cell carcinoma metastatic to a cervical lymph node is usually responsive to irradiation therapy. However, most therapists and surgeons agree that irradiation has a low rate of success in curing nodes larger than 3 centimeters in diameter. For patients with nodes larger than 3 centimeters, the primary form of treatment is radical neck dissection, with or without pre- or post-operative irradiation

therapy.

The radical neck dissection is intended to remove all diseased lymph tissue from the neck. It is frequently performed in conjunction with radical removal of the cancer in the primary site so that the entire specimen can be resected en bloc. Ideally, the primary, the nodes, and all the lymphatic channels connecting them are removed without cutting across any of them. The sternocleidomastoid muscle and the jugular vein are usually taken with the lymph nodes since the major beds of lymph nodes abut these two structures. A patient can function well without the muscle, vein, and nodes. This leaves the carotid artery and its bulb on the floor of the neck to be covered only by skin flaps. Normally, skin is a sufficient covering for the carotid, but in a patient with head and neck cancer, the skin of the neck must often undergo considerable "abuse." More often than not it must withstand irradiation therapy. Not infrequently, resection of a squamous cell mucosal lesion results in a fistula from a mucosal wound to the skin. From the fistula, oropharyngeal and sometimes tracheal secretions pour across the skin.

One of the dreaded complications of radical neck surgery is rupture of the carotid artery (carotid blowout). When the carotid is covered with healthy skin, this virtually cannot happen. But if the skin over the carotid breaks down because of tension on a suture line, loss of vascularity, irradiation devitalization, or infection from a fistula, carotid blowout becomes an immediate life-threatening possibility. For this reason, the incisions for radical neck dissection have been designed to prevent skin loss, and to keep healthy skin over the carotid even if a suture line does break down. No one has yet designed a perfect incision. None of them gives the surgeon the luxury of being able to sacrifice significant amounts of skin. If skin must be sacrificed, or if skin is lost for other reasons, the defect must be covered, usually with a skin flap from a distant site, such as the chest. The chest defect can then be covered with split thickness skin taken from the thigh.

APPROPRIATE MANAGEMENT OF AN ENLARGED CERVICAL LYMPH NODE

An enlarged lymph node in any patient might be the first sign of potentially lethal disease. It must be recognized with appropriate concern and managed accordingly. Until the managing physician is confident that the node does not represent serious disease, he must pursue his diagnostic options with reasonable haste.

A complete history and physical examination is the cornerstone of management. Certain findings, such as a long smoking history, will increase the physician's concern while directing his diagnostic work-up down certain paths. Other findings, such as a history of a recent dental abscess, will tend to allay his concern while directing his work-up toward other paths. After all the pertinent questions have been asked, a

Continued on Page 70

...in the functional bowel/irritable bowel syndrome*

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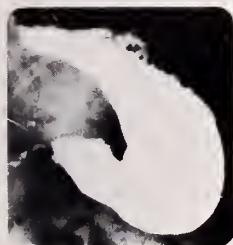
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helps control abnormal motor activity
with minimal anticholinergic side effects†

Demonstrated smooth muscle relaxant activity.

In this double-blind study, twenty patients having G.I. series and exhibiting spasm were randomly selected to receive either 2 cc. of Bentyl or sodium chloride intramuscularly. Ten minutes after the injection another radiograph was taken . . .

. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.



Pylorospasm has almost totally blocked passage of barium meal.



Barium meal beginning to pass 10 minutes after intramuscular injection of 20 mg. Bentyl.

"The correlation of spasm relief and drug given was excellent."

*This drug has been classified "probably" effective in treating functional bowel/irritable bowel syndrome.

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:

King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964.

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Brief Summary

INDICATIONS

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the following indications as "probably" effective:

For the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

THESE FUNCTIONAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS.

For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS: Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloro-duodenal stenosis), paralytic ileus, intestinal atony of the elderly or debilitated patient, unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis; toxic megacolon complicating ulcerative colitis, myasthenia gravis. **WARNINGS:** In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. **PRECAUTIONS:** Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with: Autonomic neuropathy. Hepatic or renal disease. Ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur. **ADVERSE REACTIONS:** Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia, urinary hesitancy and retention; blurred vision and tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste; headache; nervousness, drowsiness; weakness; dizziness, insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. **DOSE AND ADMINISTRATION:** Dosage must be adjusted to individual patient's needs.

Usual Dosage: Bentyl 10 mg capsule and syrup. **Adults:** 1 or 2 capsules or teaspoonfuls syrup three or four times daily. **Children:** 1 capsule or teaspoonful syrup three or four times daily. **Infants:** ½ teaspoonful syrup three or four times daily. (May be diluted with equal volume of water.) Bentyl 20 mg. **Adults:** 1 tablet three or four times daily. Bentyl Injection. **Adults:** 2 ml. (20 mg) every four to six hours intramuscularly only. **NOT FOR INTRAVENOUS USE.** **MANAGEMENT OF OVERDOSE:** The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine[®] (bethanecol chloride USP) should be used.

Product Information as of October, 1978

Injectable dosage forms manufactured by CONNAUGHT LABORATORIES, INC., Swiftwater, Pennsylvania 18370 or TAYLOR PHARMACAL COMPANY, Decatur, Illinois 62525 for MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc., Cincinnati, Ohio 45215, U.S.A.

thorough physical examination must be performed. Since most pathological processes giving rise to enlarged cervical nodes begin in structures above the clavicles, the examination should be most detailed in the head and neck. Otolaryngologists are skilled in examining recesses of the head and neck that cannot be seen with the armamentarium available to most physicians. It is, therefore, highly appropriate to consult an otolaryngologist in these cases. But the rest of the body must not be ignored. Neck metastases from distant organs do occur. Also, finding enlarged nodes below the clavicles can be very important.

With a firm data base of history and physical examination, the physician must decide on the next step in management. Frequently, the physician is confident that the enlarged node was caused by a previous inflammatory process, and that it is safe to do nothing more than observe the node for a period of time. If not, he must begin a diagnostic work-up. As the data accumulates, he might at any time arrive at a firm diagnosis or at the point of confidence that the node is simply a reaction to inflammation. At some point he might decide that a tissue diagnosis is required. This is the time when consultation with an otolaryngologist or other head and neck surgeon is mandatory, if it has not already been done.

In many of these cases, it seems that the most diagnostic and most readily available tissue is the enlarged node itself. In fact, the node is rarely the most diagnostic tissue. In 90 percent of cases of metastatic carcinoma, the tissue type is squamous cell. This information does not help at all to locate the primary disease process. The node is frequently not the most readily available tissue, either. Most squamous cell carcinomas originate in the aerodigestive tract and the primary cancer can be easily biopsied with a cupped forcep through the mouth or nose directly or through an endoscope. These are very good reasons not to biopsy the node. *But the most important reason not to biopsy the node is that such an action will significantly compromise the prognosis of a patient with head and neck carcinoma.*

Open biopsy of a neck node containing metastatic carcinoma usually spills cancer cells into the operative field, and might even "pump" them through the blood or lymphatic systems to distant sites. The operative field can be treated, once the diagnosis is made, by wide-field excision or irradiation, but this involves needless sacrifice of, or trauma to, important neck tissue. If a radical neck dissection is to be performed on a neck which has undergone previous open biopsy, multiple problems beset the surgeon. He must resect the skin and soft tissues around the previous biopsy site in continuity with neck specimen without compromising the vascularity of the neck flaps and without placing the carotid artery in too vulnerable a position. Frequently, a skin flap rotated from a distant site (the chest) is required to cover the carotid artery.

Irradiation therapy is less effective in a scarred operated field because of reduced vascularity and reduced availability of oxygen to form free radicals.

Merrell

MERRELL-NATIONAL LABORATORIES
Division of Richardson-Merrell Inc.
Cincinnati, Ohio 45215 U.S.A.

"Renewed activity in the neck of a patient with a previously excised lymph node invariably occurs in the region from which the node has been excised for diagnostic purposes."³

I do not think that a percentage can be assigned to the reduction in survival of patients who have had a premature biopsy. Publication of a series of patients might open a Pandora's box of litigation, and I know of no such series. But anecdotal evidence abounds. The experts agree, premature biopsy is a serious mistake.

Before even considering an open biopsy, all reasonable diagnostic studies should be undertaken. Special care must be exercised when the node is in the supraclavicular fossa, area 6. "The search is directed toward the upper esophagus, lung, breast, thyroid gland, stomach, ovary, prostate, colon/rectum, biliary sites, pancreas, uterus, liver, and kidney."⁴ For an enlarged node in area 6 or any other area of the neck, "laboratory procedures include routine blood studies, chest x-ray, sinus x-rays, and if indicated, contrast studies of the gastro-intestinal tract and intravenous pyelogram. A radioactive thyroid scan is also obtained. If there are still no clues as to a possible primary site, endoscopic examinations are performed. These include: laryngoscopy, bronchoscopy, and esophagoscopy. Random biopsies are obtained from the nasopharynx, base of tongue, tonsil, and any other suspicious areas in the hypopharynx or larynx. If these biopsies are normal, an open biopsy of the neck with frozen section, or a needle aspiration, or Silverman needle biopsy is then performed. ...a negative needle biopsy does not exclude metastatic disease and an open biopsy should then be performed. If indicated, a radical neck dissection is performed at the time of open biopsy depending on the histology of the neck mass on frozen section."⁴ Only if all of the pathology specimens and lab tests fail to reveal the origin of the cancer can it be considered a metastatic carcinoma with an unknown primary.

Appropriate therapy can be with surgery, irradiation therapy, or combinations of both. The survival rate for patients with an undetected primary is from 14 percent⁵ to 37 percent.⁶ These figures are considerably worse than the overall figures for most types of head and neck cancer. Obviously, a patient can receive more appropriate treatment if the full extent of his disease is known prior to treatment, and knowing the full extent of disease obviously includes knowing the primary. If the original search fails to uncover the primary, the search should be repeated at intervals.

IMPORTANT CLINICAL CLUES

There are several findings that should arrest the at-

tention of any physician. They are: (1) A long history of smoking. This makes the diagnosis of squamous cell carcinoma very probable. (A negative history for smoking makes squamous cell carcinoma of the mouth, pharynx, and larynx unlikely, but is not a mitigating factor against carcinoma of the nasopharynx or paranasal sinuses.) (2) Nodes in area 5 of the posterior triangle. They are almost always metastatic from a primary in the nasopharynx. (3) Unilateral serous otitis media. If it is not explained by a recent nasopharyngeal obstructive problem such as a URI, it should be considered evidence of nasopharyngeal carcinoma until proven otherwise. (4) Any enlarged node whatsoever in areas 1, 3, 4, 6, 8, or 9. Inflammatory processes causing enlargement of these nodes are very rare compared to malignant processes. In adults and children, some adenopathy frequently occurs in areas 2 and/or 5 during and after a simple URI. Enlargement of the submandibular gland and the nodes around it can occur with dental problems or duct obstruction. Area 10 nodes can enlarge in response to otitis externa. But there are no common inflammatory processes that cause swelling in the other areas of the neck. (5) A rock hard node. This is almost universally metastatic in nature.

SUMMARY

An enlarged cervical lymph node can be the first sign of a potentially lethal disease. In adults, and particularly in smokers, an item high on the differential diagnosis must be head or neck carcinoma. The temptation to biopsy the node to make the diagnosis must be resisted until complete laboratory, radiologic, and endoscopic evaluation has failed to reveal a primary carcinoma. Even then, the biopsy must be done with care, preferably by the surgeon who will perform a radical neck dissection should the node contain carcinoma. Premature biopsy of a cervical node does considerable harm to the patient.

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Computed Tomography of the Chest

BARRY KUTZEN, M.D.*

INTRODUCTION

Computed tomography can provide us with unique information because it demonstrates anatomy in a transverse plane free of overlying structures and is able to distinguish previously undetectable differences in radiographic density. In certain situations CT of the thorax may provide us with significant information that is unobtainable by conventional radiographic techniques. In addition, CT offers precise localization information so that proper biopsy procedures can be instituted in an optimal manner. Staging of certain neoplastic processes is sometimes possible without further intervention.

MATERIAL AND METHODS

Examinations were performed at the Central Maine Medical Center on a Pfizer 0200 FS whole body unit using either 29 or 19 second mode in suspended (when possible) or quiet respiration. All patients had high KV PA and lateral chest films and in addition some had conventional whole lung and hilar tomography prior to the CT. For masses in the paramediastinal area or of a suspected vascular nature Renografin® 60% (E.R. Squibb) 100 cc. was injected intravenously as a bolus and rapid sequence images obtained.

CASE PRESENTATIONS

1. A 52-year-old female with fibrosarcoma of her leg discovered in April 1979. Chest film and whole lung tomograms demonstrated no abnormalities. Chest CT (Fig. 1) done one month later (just after installation) demonstrates multiple small pulmonary nodules consistent with metastatic disease. Chest film in September 1979 and percutaneous biopsy confirmed metastatic fibrosarcoma.

COMMENT

The sensitivity of CT in detecting pulmonary nodules has been widely demonstrated.^{3,6} CT can demonstrate pulmonary nodules in up to 50% of patients suspected of having pulmonary metastases with normal chest radiographs and additional lesions in those with one or more lung nodules seen on conventional films.⁴

2. A 67-year-old male treated symptomatically for six months for back pain. Chest film on admission revealed a right upper and paramediastinal mass. CT (Fig. 2) revealed the lesion to have invaded and destroyed the adjacent rib and vertebral body and was invading the neural canal. Percutaneous skinny needle aspiration biopsy yielded epidermoid carcinoma.

COMMENT

The vertebral body destruction and invasion of the neural canal demonstrated by CT would be difficult to image by conventional means because of the purely lytic nature of the process. Bone scan was also negative. Proper therapy decisions were made based on demonstration of neural canal involvement.

3. A 55-year-old male with previous pneumonectomy for carcinoma of the lung 6 years prior to admission. The patient had a

fever of unknown origin for several months prior to evaluation. Chest film demonstrated total opacification of the left hemithorax. Gallium 67 images demonstrated some increased activity in the left hemithorax. CT (Fig. 3) demonstrated an area of low attenuation surrounded by a rim of higher attenuation consistent with an abscess. Thoracentesis yielded large amounts of purulent material (empyema).

COMMENT

The ability of CT to differentiate small density differences permitted precise localization of the empyema. CT is also very accurate in identifying abnormalities of fat density in the mediastinum and differentiating cystic masses from solid lesions.

4. A 76-year-old female. Chest film demonstrated only a right hilar mass. CT (Fig. 4) provides additional information about extension of the neoplasm to involve the posterior pleura. Aspiration biopsy yielded poorly differentiated epidermoid carcinoma.

COMMENT

The ability to evaluate mediastinal and pleural extension of bronchogenic carcinoma by obliteration of mediastinal fat planes and localized pleural thickening provide the basis for a new dimension in the pre-operative evaluation and staging of bronchogenic carcinoma.¹⁵

5. A 72-year-old female with weakness and lethargy. Chest film demonstrated mediastinal widening and left hilar mass. CT (Fig. 5) following 100 cc. of Renografin 60 demonstrates a dissecting aneurysm (type I) and fresh blood in the pleural space consistent with recent hemorrhage.

COMMENT

The diagnosis of a dissecting aneurysm is not always as obvious as in this clearly demonstrated case. Trauma victims can have mediastinal contour changes secondary to venous bleeding as well as aortic injury. The CT scanner offers an alternative to angiography in selected cases and will on occasion prevent the unnecessary performance of more expensive and potentially dangerous angiographic analysis.

SUMMARY

There are limitations:

1. Small lymph nodes around the hilus may not be detected, and hilar tomography (55° oblique) remains a good alternative.
2. Small parenchymal scars may be over diagnosed as metastatic lesions.
3. Because of continued movement of cardiac chambers, current CT scanners can only grossly examine the heart.
4. Esophageal mucosal lesions are better demonstrated by double contrast barium evaluation.

ADVANTAGES

1. Evaluation of masses of fat density.
2. Evaluation of pneumonectomy sites.
3. Evaluation of aortic aneurysm, periaortic hematoma and hemorrhage.
4. Extent of lesions involving the chest wall.
5. Differentiation of cystic versus solid masses.
6. Staging of bronchogenic carcinoma.

*Central Maine Medical Center, Lewiston, Maine 04240.

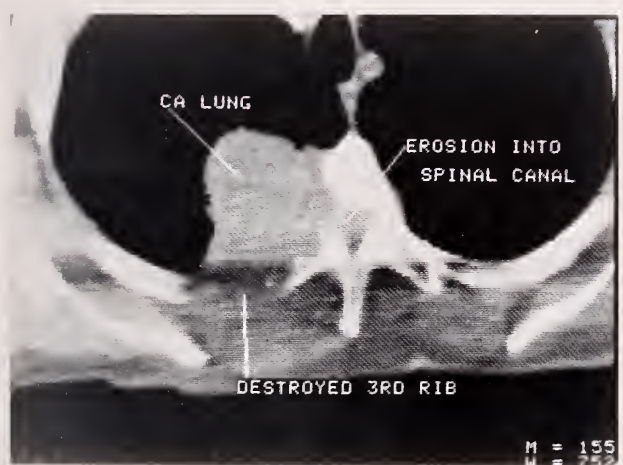


Fig. 2

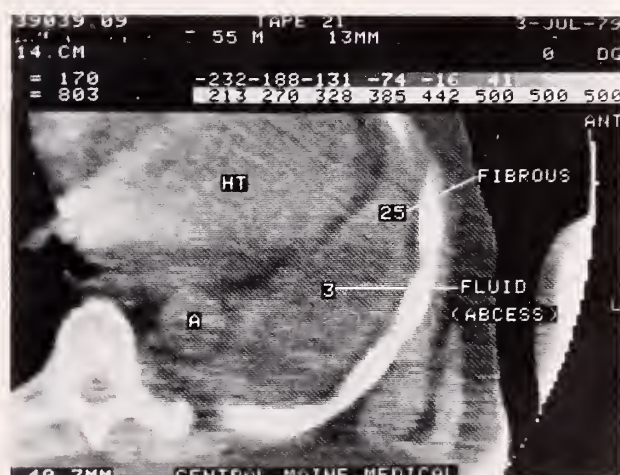


Fig. 3

CONCLUSION

CT of chest can provide unique diagnostic information not available by conventional techniques. The cost (\$225) compares favorably with other diagnostic procedures. When utilized with skinny needle aspiration biopsy, it provides a rapid means of diagnosing and staging intrathoracic neoplasms in selected patients with less expense and morbidity to

7. Evaluation of lung for metastatic nodules.
8. Evaluation of mediastinum when plain films are equivocal.
9. Accurate placement of needle for aspiration biopsy.
10. Differentiation of benign versus malignant nodules in selected cases by tissue attenuation characteristics.

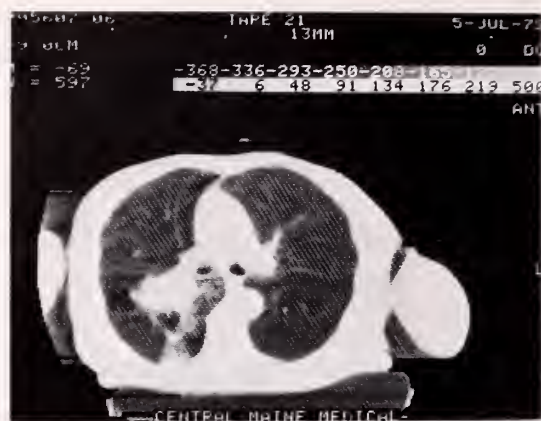


Fig. 4

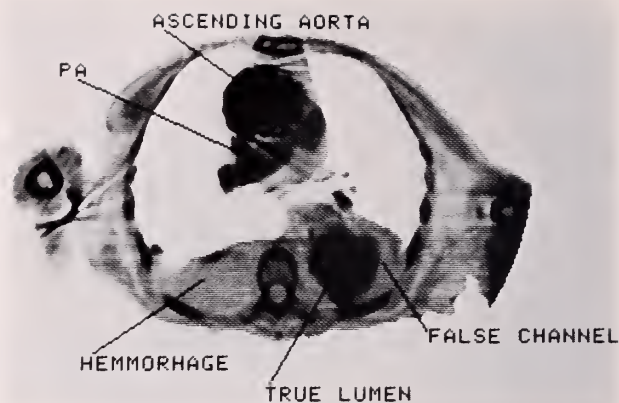


Fig. 5

the patient than currently available methods, and in this regard, it is certainly complementary to bronchoscopy and mediastinoscopy. The incremental information made available makes this a valid and important means of aiding in the diagnosis of diseases of the chest.

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CONTINUING MEDICAL EDUCATION IN MAINE—Continued from Page 95

Northern Maine Medical Center Fort Kent, Maine

April 14, 1980
10:30 a.m. **Infectious Diarrhea**
John Bartlett, M.D., Tufts University School of Medicine, Boston, Massachusetts
This program has been certified AMA and LCCME Category I. For further information contact Kenneth D'Amato, D.O.; 444-5973.

Penobscot Bay Medical Center Rockland, Maine

April 11, 1980
11 a.m.-12 Noon **Subject to be announced**
Tufts University School of Medicine
This program has been certified AMA and LCCME Category I. For further information contact Lloyd Roberts, M.D.; 594-9511.

Regional Memorial Hospital Brunswick, Maine

April 15, 1980
Infectious Diseases
Speaker to be confirmed
This program has been certified AMA and LCCME Category I—1 hour.
For further information contact Gerry S. Hayes, M.D.; 729-0181.

V. A. Hospital Togus, Maine

General Staff Meetings
March 31, 1980
2 p.m. Laboratory Service
Subject/speaker to be announced
April 8, 1980
Medical Service

12 Noon
Subject/speaker to be announced
May be viewed over ITS

April 14, 1980
2 p.m. Research Service
Subject/speaker to be announced
April 21, 1980
2 p.m. Assistant Chief of Staff
Subject to be announced

Medical Service Staff Meeting

Every Wednesday
1:15 p.m. Subjects to be announced

Oncology Clinic

Every other Thurs.
2 p.m. Subjects to be announced

Neurology Lecture

Neurobehavior
March 21, 1980
11 a.m. Michael Alexander, M.D., Director, Behavioral Unit, Boston VA Hospital
May be viewed over ITS

April 18, 1980
11 a.m. Subject to be announced
Bennett Stein, M.D., Professor & Chairman, Department of Neurosurgery, New England Medical Center and Tufts Medical School

These activities have been certified AMA and LCCME Category I. No registration fee. For further information contact E. Osborne Coates, M.D., VAM and ROC, Togus; 623-8411.

ANNOUNCEMENT: Medical Care Development, Inc. is now receiving a listing of continuing medical education activities taking place in Vermont, New Hampshire, and Massachusetts. If you wish further information contact Gerald Gould, Medical Care Development; 622-7566.

Computed Tomography of the Pancreas

RUSSELL V. RADCLIFFE, M.D.*

INTRODUCTION

The pancreas has long been referred to as the "hidden organ." Until the last few years, a non-invasive work-up was limited to laboratory studies or indirect imaging techniques, such as hypotonic duodenography or the routine upper gastrointestinal series. More recent invasive techniques such as angiography and ERCP have offered significantly more specific information, but suffer the difficulty of selected application against a background of large numbers of patients having possible but undefined pancreatic abnormality.

Recent development of non-invasive pancreatic imaging has centered around ultrasound and computed tomography (C.T.). Both imaging modalities have undergone marked refinement within the last five years. Studies from major ultrasound centers report a visualization rate of 94% (not including the tail of the pancreas), particularly when upright scanning through the water-filled stomach and repeat studies on several days are used.^{1,2} Our local experience has not matched these inspiring results.

The initial limitations² of pancreatic C.T. have yielded to refinements in use of contrast and glucagon, shorter scanning times, definition of normal anatomy as seen by C.T., and increasing user experience.³ The literature reflects C.T. pancreatic accuracies of over 90% with 3% false negatives and 2% failed studies;⁴ with careful application these figures are readily obtainable at a community medical center.

PROCEDURE

Upper abdominal body scanning is performed after consultation, with similar preparations for out- and in-patients.

1. 15 cc. of Gastrografin® diluted in 400 cc. of Tang-flavored water is given orally the evening prior to the examination. This places contrast in the colon.
2. 12 cc. of Gastrografin diluted in 400 cc. of Tang/water is given orally 30-45 minutes before the study to assure contrast in the stomach and upper small bowel.
3. Sections through the area of interest are obtained to evaluate for abnormality and to permit selection of optimal levels for detailed evaluation following intravenous contrast administration.
4. 100 ml. of Renografin® M-60 is given rapidly intravenously in combination with 1 mg. glucagon (except when contraindicated), and appropriate

sections through the area of interest are obtained.

All studies are performed on our Pfizer 0200FS body scanner, using a 13 mm. section width and 18 or 28 second scanning time, depending on the patient's ability to suspend respiration. Generally pre-contrast sections are obtained at 2 cm. intervals, but usually 1 cm. intervals are needed for post injection full pancreas visualization, and occasionally supplemental sections 5 mm. apart are needed. A radiologist directly supervises each study, and at our institution all radiologists and other interested physicians review each study the following morning, increasing diagnostic accuracy and broadening our experience. No gantry tilt is used, as this would cause magnification.

Accurate measurements are available for pancreas evaluation,⁵ indicating upper normal limits (plus one standard deviation) of 26 mm., 23 mm., and 17.5 mm., for width of the head, body, and tail. Precise application of these measurements has permitted accurate diagnoses of mild diffuse enlargement and tail enlargement in two cases. It is essential to identify adjacent structures separately so that they are not inadvertently included in the measurements;⁶ usually contrast in the duodenum and splenic vein suffice (see Figures A and B). Since the pancreas is almost never fully imaged on one section, measurements must be obtained in most cases on several adjacent images.

Rarely a patient will present with so little retroperitoneal fat that the precise pancreatic measurements are difficult to obtain. Usually indentification of contrast-filled adjacent structures and measurement of the residual "pancreatic space" will suffice to exclude enlargement or mass. Obviously, atrophic chronic pancreatitis could be missed in this circumstance unless calcifications or duct dilatation are seen.

MATERIAL

From March 1, 1979, through October 31, 1979, 47 patients have been studied with C.T. at the Central Maine Medical Center for possible pancreatic disease, or 5% of our case load. Additionally the pancreas is routinely imaged whenever adjacent structures (liver, spleen, retroperitoneum, kidneys, or adrenal glands) are specifically studied. Of these 47 studies, 26 have been found to be normal. Twenty-one have been abnormal, and of these several represent repeat studies for follow-up of pancreatitis or, in one instance, radiation therapy planning (See Table 1).

All of the patients in the "mass" classification have undergone confirmation by evidence of liver metastases (see Figure C), aspiration needle biopsy, open biopsy, or clinical course.

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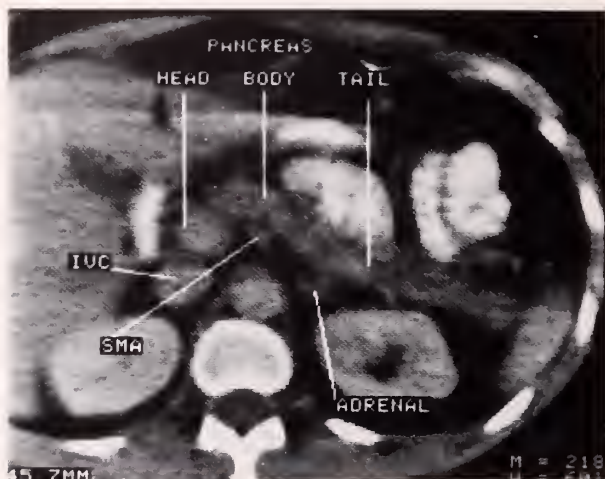


Fig. A



Fig. B

Figure A demonstrates many of the normal upper abdominal structures prior to intravenous contrast administration.

Figure B taken at a slightly different level following intravenous contrast administration, demonstrates the intimacy of the splenic vein and the pancreas.

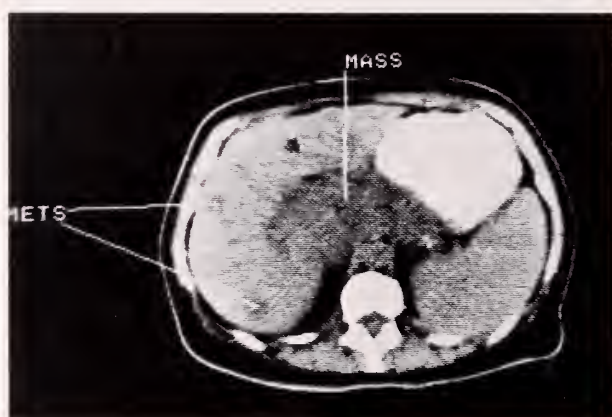


Fig. C

Figure C demonstrates the presence of a large pancreatic mass obliterating most of the adjacent anatomy, and demonstrates metastases in the liver, confirming a carcinoma.

In our series the computed tomographic evaluation has never failed to provide an adequate study of the pancreas and adjacent organs.

DISCUSSION

Most computed tomography studies of the pancreas are requested to evaluate for possible mass, reflecting carcinoma, pancreatitis, or sequelae (pseudocyst or abscess). Other authors³ have reported on potential pitfalls in C.T. diagnosis of the pancreas. These range from failure to use adequate contrast material, failure to properly monitor the study, and inexperience; to more difficult problems like the presence of extensive abnormality in the adjacent structure obliterating landmarks. One recent case at our institution proved this point, with a large lesser sac abscess masquerading as a pancreatic mass.

Early articles comparing ultrasound to C.T. described limitations to C.T. diagnosis attributable in part to patient motion.⁴ With 18 second or less

TABLE I

Pancreatic mass (carcinoma or inflammation)	13
Chronic pancreatitis	4
Radiation therapy planning	1
Normal pancreas, other organ abnormal	3
Kidney	1
Liver mass	1
Lesser sac	1

scanning time and generally cooperative patients, respiratory motion has never been a problem in our series. The presence of residual barium resulted in one suboptimal but adequate study, and required rescheduling a patient on another occasion. Surgical clips are a potential source of difficulty, but thus far, have never precluded adequate evaluation. Absence of fat may complicate the study, but generally identification of other normal landmarks⁴ (See Figures A and B) and measurement of the "pancreas space" will exclude mass lesions in these cases.

When C.T. reveals evidence of pancreatic calcification, parenchymal atrophy or ductal dilatation reflecting chronic pancreatitis, as in four of our cases, a diagnostic end-point is reached, of more value than a "normal" upper G.I. study, liver scan, or other indirect, non-invasive study. When a normal C.T. study is obtained in a patient with questionable but suggestive symptoms of pancreatic disease, another type of end-point is reached. When a definite mass is demonstrated, the non-invasive C.T. evaluation will direct further management, be it aspiration biopsy, expectant management, or surgical intervention.

CONCLUSION

By careful adherence to established techniques, computed tomography of the pancreas offers a highly sensitive and specific assessment of the organ.

Continued on Page 81

Prophylactic Lidocaine in the Early Management of Acute Myocardial Infarction

LARRY O. HOPPERSTEAD, M.D.* AND MARY H. MYERS, R.N., B.S.N.**

ABSTRACT

There is a high incidence of fatal ventricular dysrhythmias occurring without warning during the first few hours of an acute myocardial infarction. Several investigators have recently shown that prophylactic lidocaine can effectively reduce the incidence of primary ventricular fibrillation in acute myocardial infarction patients, thus decreasing early and late mortality. It has been documented that the rapid achievement of therapeutic plasma lidocaine levels within the first few minutes of treatment is effective at preventing primary ventricular fibrillation. This paper discusses a safe and effective method of achieving therapeutic plasma levels with an initial loading dose of 250 to 300 mg within 16-21 minutes, using multiple intravenous boluses. We recommend that lidocaine be used prophylactically in situations of proven or suspected acute myocardial infarction, and that treatment be initiated immediately upon making that distinction.

INTRODUCTION

One of the inescapable lessons in this the age of Coronary Care Units (CCU) and Advanced Prehospital Coronary Care is that in the first few hours of an acute myocardial infarction (AMI) the heart is at its most vulnerable risk. The incidence of death in AMI is greatest in the first 60 minutes, but remains high for the first 2-4 hours, after which it falls off dramatically.^{1,2} This early vulnerability is even more pronounced for the young victim of his first AMI.³ Most of those early deaths, which account for better than 50% of all deaths attributable to AMI yearly, are a result of the development of primary ventricular fibrillation (VF) as a complication of AMI.¹

It was primarily for the early detection and treatment of VF that CCU's were developed in the early 1960's, using electrical monitoring, cardiopulmonary resuscitation, and defibrillatory countershock to reverse this lethal dysrhythmia. By the mid-1960's, the efficacy of lidocaine in suppressing ventricular dysrhythmias associated with AMI, and therefore preventing development of VF, had been established.⁴ Its use was generally restricted, however, to those patients who had demonstrated the so-called "warning arrhythmias" as defined by Lown in 1967; namely, frequent premature ventricular contractions

(PVC's), R-on-T phenomenon PVC's, coupled PVC's, multifocal PVC's, or short runs or bursts of two or more PVC's.⁵

During the past decade, more intensive observation and monitoring of patients in the initial stages of AMI (both in the CCU and in the prehospital setting) have clearly demonstrated two facts. First, even in the best of CCU's, from 25-50% of all initial incidences of VF are not preceded by a clearly defined or detected warning dysrhythmia.⁶ Second, in the initial crucial hours of AMI, warning dysrhythmias are less likely to occur prior to the development of VF, and when they do, there is likely to be only an extremely short period between the warning dysrhythmia and the subsequent VF.⁶ It has thus become obvious that reserving anti-dysrhythmic treatment only for those who develop warning dysrhythmias leaves a large number of potential VF patients unprotected. Furthermore, recent studies have shown a high correlation between VF cardiac arrest during AMI and increased death rates both during and after hospitalization.^{7,8} This fact is regardless of the proficiency and effectiveness of the resuscitation events, so it appears that the fibrillatory occurrence itself is the cause of the increased mortality. Accordingly, many authorities are now advocating the early use of lidocaine in AMI, whether or not warning dysrhythmias are present, as prophylaxis against the development of lethal primary VF.⁹⁻¹⁴

Whereas initially it was felt that lidocaine was less effective in the first few hours of an AMI at preventing the development of primary VF, with better understanding of lidocaine pharmacokinetics, it now appears that those early "failures" in lidocaine therapy were secondary to having sub-therapeutic plasma levels on board in the initial stages of treatment.⁹ This paper presents an effective methodology for assuring appropriate lidocaine levels from the very onset of treatment, and for preventing the development of a "sub-therapeutic hiatus" shortly after initiation of treatment. As such, it presents a methodology to reduce the incidence of primary VF in AMI, thus enhancing the survival potential of patients with AMI.

EFFECTIVENESS OF PROPHYLACTIC LIDOCAINE

A number of studies support the theory that lidocaine will prevent the development of VF and decrease the number of PVC's if given prophylactically to patients with suspected AMI, that is, before their development of premonitory dysrhythmias. Wyman and Hammersmith snowed in a study of 1,165 con-

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**Education Coordinator, Emergency Medical Services, Central Maine Medical Center, Lewiston, Maine 04240.

secutive AMI patients a reduction in the incidence of primary VF from 6.5% of 139 cases not treated prophylactically to 0.3% of 1,026 cases treated prophylactically.¹⁰

Pitt, et al, evaluated 222 patients with AMI. Lidocaine was given prophylactically to 108 subjects on admission, with 114 patients matched as controls. Lidocaine therapy was begun or increased for "tachydysrhythmias" in both groups. Nonetheless, frequent PVC's, salvos, and ventricular tachycardia were observed in only 10% of the prophylactically treated group as opposed to 30% of the control group.¹¹

The most conclusive study that prophylactic lidocaine therapy reduces the incidence of primary VF in AMI patients was performed by Lie, et al. This double-blind, randomized study, evaluated 212 consecutive AMI patients under the age of 70, all who were admitted to the hospital within six hours of the onset of their AMI symptoms. Of the 107 patients who received lidocaine prophylactically, *none* experienced primary VF. However, of the 105 patients who received a placebo infusion, nine experienced primary VF. The study was statistically significant to the $p < 0.002$ level.¹²

LIDOCAINE PHARMACOKINETICS

The effectiveness of lidocaine therapy is based on the capability of developing therapeutic plasma levels of the drug rapidly, and then maintaining those same therapeutic levels. According to most authorities, the therapeutic range is approximately 2.0-5.0 $\mu\text{g/ml}$.^{15,16} Presently, the accepted standard to institute lidocaine therapy is an intravenous (IV) bolus of 75-100 mg, followed by a constant IV drip of 2-4 mg/minute. This technique provides an initial (almost immediate) plasma level in the therapeutic range, but within a few minutes lidocaine levels become sub-therapeutic and may remain that way for several hours.¹⁷ The plasma levels attained by the initial bolus fall off rapidly, while the levels to be attained by the constant IV drip build up very slowly.

The reason for the above-identified problem is that the standard approach to lidocaine therapy does not take into appreciation the difference in half-life of lidocaine during its initial "distributive" phase and the later "eliminative" phase. In the distributive phase, the initial IV bolus of lidocaine is rapidly distributed between the plasma and highly perfused tissues such as the brain, lungs, heart, liver, and kidneys, reaching maximal drug concentrations in those organs almost immediately. As the distribution continues into the less highly perfused tissues, such as muscle and fat, the plasma concentration falls off rapidly, with its half-life for this phase being in the range of eight minutes for individuals with normal cardiac output and liver function.¹⁸ The eliminative phase of lidocaine disposition, i.e., that which comes into play after the drug is uniformly distributed throughout the body's various perfusion beds, has a half-life dependent primarily on the rate of liver per-

fusion and metabolism, with an approximate duration of 90 minutes.¹⁹ Wyman predicts that with the eliminative phase half-life of 90 minutes, it would require between five and seven hours of a constant rate infusion of lidocaine before a plasma concentration plateau would be reached where rate of drug input would just equal rate of elimination.¹⁷

TECHNIQUES OF LIDOCAINE ADMINISTRATION

The therapeutic implication of the lidocaine pharmacokinetics described above is that large amounts of the drug must be given in the initial stages of therapy in order to achieve and maintain therapeutic plasma levels. Yet, at the same time, it is obviously desirable to avoid the potentially deleterious effects of toxic plasma levels. The approaches developed to meet these conflicting needs of the early treatment stage have included multiple initial IV boluses spaced 5-10 minutes apart, initial large-dose constant rate infusions, and large dose intramuscular (IM) injections. Each approach is linked to the simultaneous establishment of an on-going, low-dose, constant rate infusion (typically 2-4 mg/minute) to continue for the desired duration of therapy. Whatever the methodology, the initial 20 minutes of treatment seem to be the crucial ones. In those first 20 minutes, the essential goal is the administration of a loading dose of 200-300 mg of lidocaine, depending on the size of the patient.

The multiple IV bolus approach is propounded by Harrison and by Wyman, et al. Harrison recommends either a 100 mg bolus given over two minutes' time and repeated ten minutes later, or a 50 mg bolus given over one minute and repeated three times at five minute intervals.⁹ In the first situation, 200 mg would be infused in 12 minutes, in the second, 200 mg would be infused in 16 minutes. Wyman's approach is similar, with an initial 75 mg bolus over one minute, and three additional boluses of 50 mg each given at five minute intervals thereafter.¹⁷ Thus 225 mg is infused in the first 16 minutes. Both investigators start a low-dose, constant rate infusion of 2-4 mg/minute simultaneously with the initial loading dose, so that the total lidocaine dose received in the first 20 minutes of therapy is 40-80 mg higher than that from the boluses alone.

Initial large-dose, constant rate infusions have been advocated by Levy, et al, and by Campbell, et al. Levy's group utilizes a loading infusion rate of 25 mg/minute, and runs it to a total of 200 mg (eight minutes) for patients < 68 kg, to 250 mg (ten minutes) for patients weighing 68-90 kg, and to 300 mg (12 minutes) for patients > 90 kg. They then start a low-dose, constant rate infusion.²⁰ Campbell's group, in comparison, combines an initial loading bolus of 75 mg IV with an infusion of 10 mg/minute for 20 minutes, then following with a low rate infusion of 1.5 mg/minute, thus giving a total dose of 275 mg in the first 20 minutes.²¹ In both approaches, it is imperative to use infusion pumps for accuracy and safety.

Each of the above investigators was able to demonstrate plasma lidocaine levels in the therapeutic range throughout the "loading" phase of treatment. There was no sub-therapeutic hiatus, as with the standard approach to institution of lidocaine therapy. And there were only moderate, easy to control, infrequently occurring side effects, typically mild confusion, drowsiness, and/or light headedness, for the plasma levels stayed significantly below the toxic range. The key to the prevention of side effects appears to be *not exceeding* an infusion rate of 50 mg/minute by whatever means. The total doses given over the first 20 minutes of therapy, figuring an infusion rate of 2 mg/minute in addition to the loading doses, are as follows:

Harrison — 240 mg	Campbell — 275 mg
Wyman — 265 mg	Levy — 270 mg

All the investigators make the point, which is most clearly stated by Harrison, that in situations of congestive heart failure (CHF), shock, or chronic liver disease, both the loading and maintenance doses of lidocaine should be halved to prevent severe toxic reactions.⁹ This is also the case for patients over 70 years of age. For this group, lidocaine should probably be reserved for therapeutic, not prophylactic use. Patients 70 years of age or older are much less likely to develop primary VF as a consequence of AMI,¹² while at the same time they are much more likely to develop toxic side effects from lidocaine therapy.

An alternate method of administering lidocaine prophylactically is by large-dose intramuscular (IM) injection. This method has been reserved primarily for prehospital use. According to a study by Valentine, et al, large dose IM lidocaine injections provide adequate protection against the development of VF in AMI patients during transfer to the hospital.²² He has shown that within 15 minutes of the IM administration of lidocaine 300 mg, plasma levels will be in the therapeutic range and will remain there for two hours. This assumes adequate perfusion of the tissue injection site. Therefore, patients in shock or with markedly altered perfusion status would not be candidates for this route of administration.

A double blind study by Lie, et al, contradicts Valentine's findings by showing lidocaine 300 mg IM to be ineffective in preventing VF during the first hour of AMI. Lie's work demonstrated sub-therapeutic or marginally therapeutic levels of lidocaine throughout the first hour following IM injection, and demonstrated no decreased incidence in the development of primary VF for treated versus control patients.²³

Alternatively, Sheridan, et al, have studied an approach to lidocaine prophylaxis which combines a loading IV bolus of 100 mg of lidocaine with a simultaneously administered IM injection of 300 mg of the drug into the deltoid muscle. With this method, effective plasma levels are attained within one minute and remain so for more than two hours. It is important to note that for the first 60 minutes,

plasma levels remain in the high therapeutic range, varying between 3.4-5.7 $\mu\text{g/ml}$.²⁴ This would appear to be a very promising method for lidocaine prophylaxis in the situation of transfer of an AMI patient from his/her home or from the physician's office to the hospital, especially in those situations where an advanced life support-trained ambulance crew capable of managing IV drips or administering medications is not available. As such, it has appeal to the practice of aggressive medicine in a highly rural environment.

RECOMMENDED PROTOCOL FOR THE ADMINISTRATION OF LIDOCAINE

We have developed a standard protocol for the administration of lidocaine to patients with proven or suspected AMI, which can be used both "prophylactically," i.e., to prevent the development of ventricular ectopy and tachydysrhythmias, and "therapeutically," i.e., to control any pre-existing ventricular warning or tachydysrhythmias. The protocol takes into account the necessity for early, aggressive anti-dysrhythmic therapy to be administered in a safe, standardized method. It incorporates prehospital, as well as Emergency Department institution of therapy, utilizing Advanced-EMT Cardiac Technicians in the prehospital setting. The goal is to prevent the development of primary VF in this vulnerable group of patients, thereby markedly increasing their short- and long-term survival rates.

We have chosen the multiple bolus technique for instituting the loading dose of lidocaine because we feel it is the safest and most effective method. We combine this with a simultaneously administered low-dose, constant rate infusion to be continued for the course of therapy, typically 24-48 hours, but which can be stopped abruptly at any time. Our lidocaine administration protocol is outlined below and is started as soon as the distinction of proven or suspected AMI is made:

LIDOCAINE REGIMEN

- A. **LOADING DOSE** (Objective is to administer 250 mg in 16 minutes)
 1. Initially, lidocaine 100 mg IV bolus over two minutes.
 2. Repeat with lidocaine 50 mg IV boluses, over one minute each, at the 5, 10, and 15 minute marks after the initial dose.
 3. If the patient weighs greater than 70 kg, give an additional 50 mg bolus over one minute at the 20 minute mark; (total dose of 300 mg in 21 minutes).
- B. **CONTINUOUS INFUSION**

—At time of initial lidocaine bolus, start an IV drip of lidocaine 2 gm in 500 cc D₅W, and infuse at 2-4 mg/minute.
- C. **PRECAUTIONS**
 1. Lidocaine boluses must be infused at a rate not to exceed 50 mg/minute.
 2. In patients with CONGESTIVE HEART

FAILURE, SHOCK, CHRONIC LIVER DISEASE, or OVER 70 YEARS OF AGE, dosage must be HALVED.

3. Withhold for patients with known allergies to lidocaine (exceedingly rare).
4. Withhold "prophylactic," but not "therapeutic," use for patients over 70 years of age.

D. INTRAMUSCULAR LIDOCAINE (for possible use in the prehospital setting)

—If unable to start an IV, the Advanced-EMT Cardiac Technician may give 300 mg IM into the deltoid muscle.

We have found the above methodology of lidocaine administration to be effective at preventing the development of primary VF in patients with AMI, as well as to be effective at suppressing ventricular ectopy and controlling ventricular tachydysrhythmias if they are present prior to treatment. The incidence of side effects has been low and very mild (typically a slight drowsiness), but we stress the absolute necessity of administering the medication no more rapidly than 50 mg/minute, as well as the necessity of halving the doses in patients with CHF, shock, or chronic liver disease, and in patients 70 years of age or older. This latter group, as stated before, are not candidates for "prophylactic" lidocaine, but are candidates for lidocaine therapeutically if warning dysrhythmias or ventricular tachydysrhythmias are present.

CONCLUSION

The most vulnerable time period for patients with AMI is in the first few hours, when dysautonomias and dysrhythmias are so prevalent.² Amongst the most insidious and lethal of these dysrhythmias are those of ventricular origin, especially VF, which can develop suddenly with no premonitory warning dysrhythmias.⁶ Once VF has developed, even if successfully resuscitated, the survival prognosis of the patient is markedly reduced.⁷

In a major, well controlled, double-blind study, Lie has shown that lidocaine given prophylactically to patients with AMI effectively reduced the incidence of primary VF to nil.¹² A less well controlled, but larger study by Wyman demonstrated a reduction in the incidence of primary VF from 6.5% to 0.3% with prophylactic lidocaine treatment.¹⁰

The effectiveness of lidocaine therapy relies on rapid achievement and maintenance of therapeutic plasma levels of the drug. The standard procedure of instituting lidocaine treatment can lead to a serious sub-therapeutic hiatus at about 15 minutes after the initial loading bolus.⁹ This unfortunately is frequently the time that the patient is being transferred from the Emergency Department to the CCU, and is thus a time that the patient is highly susceptible to dysrhythmic occurrences.

To avoid the sub-therapeutic hiatus in lidocaine therapy, a loading regimen is necessary that administers between 200-300 mg of lidocaine in the first

Continued on Page 81

Tenuate®

(diethylpropion hydrochloride NF)

Tenuate Dospan®

(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATION Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS. Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

WARNINGS. If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle, the patient should therefore be cautioned accordingly. *Drug Dependence.* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy.* Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children.* Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache, rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSEAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg tablet three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg tablet daily, swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSEAGE: Manifestations of acute overdose include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phenitoin (Regimine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdose.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc
Cayey, Puerto Rico 00633

Direct Medical Inquiries to:

MERRELL-NATIONAL LABORATORIES

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Cincinnati, Ohio 45215, U.S.A.

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20 minutes of treatment. This can be achieved by multiple IV boluses spaced 5-10 minutes apart, by large dose infusions for 10-20 minutes, or by a combination of an initial IV bolus with a large dose IM injection. In each case, the lidocaine therapy is continued beyond the loading phase with a low-dose constant rate IV infusion for the duration of treatment.

We advocate lidocaine *prophylactically* in situations of known or suspected AMI, that is, before the appearance of any of the so-called warning dysrhythmias or ventricular tachydysrhythmias. This therapy should be instituted as soon as the diagnosis of "AMI" or "probable AMI" is made. The protocol outlined is simple, effective, and safe. It can be used equally as well for instituting "therapeutic" lidocaine in situations where ventricular ectopy or tachydysrhythmias pre-exist.

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COMPUTED TOMOGRAPHY OF THE PANCREAS—Continued from Page 76

C.T. also offers the additional benefit of demonstration of adjacent anatomy. This may be invaluable for staging, exclusion of true pancreatic disease, or demonstration of other unsuspected abnormality.

Computed tomographic imaging of the pancreas is recommended as an effective, non-invasive means of organ demonstration in patients presenting with symptoms suggestive of pancreatic abnormality.

ADDENDUM

Since submission of the original manuscript, one case included in the study as a normal examination has proved to be otherwise. This is the only known false negative in the study, for a false negative rate of 2%.

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Timolol Toxicity: Ophthalmic Medication Complicating Systemic Disease

MICHAEL V. RYNNE, M.D.

The systemic toxicity of ophthalmic medication has gained new concern. A new class of medication, topical beta blockers applied to the eyes to control glaucoma, have caused major cardiac and respiratory complications. These are now reported with increasing frequency.^{1,2}

Timolol maleate (Timoptic®) is the most recently released and widely used topical beta blocker in the eye. Available in 0.25% and 0.5% drops, one drop of timolol is applied every twelve hours to the involved eye. There are broad indications for its use in glaucoma in its various forms. It has appeal because of its pupillary sparing properties. Unlike miotics, such as pilocarpine, timolol has no pupillary constricting effect or accommodative spasm.³ It has provided a new tool in glaucoma allowing deferral of surgery in many cases.

The indications for use of such medications include freedom from major cardiorespiratory disease, especially asthma and problems with heart rate and rhythm. Patients who would have adverse effects from beta blockade probably are not candidates for this drug. Individuals with a P-R interval greater than 0.25 secs.⁴ might be excluded from such medications. Zimmerman reports the decrease in resting pulse rate of up to six beats per minute with usually applied topical doses of this medication.

The following is a case report of such timolol toxicity complicating digitalis toxicity.

CASE REPORT

The 91-year-old female patient was admitted to Central Maine Medical Center with symptoms of palpitations and shortness of breath. Medications included digoxin (Lanoxin®) 0.125mg daily, furosemide 40mg per day q.d., pilocarpine 0.5% one drop in the right eye four times daily, and timolol 0.25% twice daily in the right eye. Her past history included arteriosclerotic vascular disease and previous heart failure. She had been followed for end-stage glaucoma in both eyes with vision limited to a central island in her right eye. Previously, she had had cataract surgery in her right eye with an aphakic correction.

On examination, her heart rate was irregular and varying from 35-50 beats per minute. Her blood pressure was 160/90. She was admitted to coronary care unit with diagnosis of digoxin toxicity. Her potassium was 5.3 meq/L and her BUN was 36; creatinine 1.7; serum digoxin level was 2.6 nannogram/dL (0.5-2.2ng/dL). Electrocardiogram showed slow junctional rhythm with nonconducted p waves, left bundle branch block with an anterior hemiblock.

After withdrawal of her digoxin over the next 72 hours, her pulse rate remained below 40 in the early A.M. and still had abnormal beats on the monitor. She had been taking her ophthalmic medication up to this point. An ophthalmologic consultation was requested because of suspicion that the timolol may be causing some cardiac depression. This consultation revealed significant glaucomatous optic atrophy, aphakia, and restricted field. The tensions were O.D. 19mmHg and O.S. 18mmHg by Schiotz tonometer.

After discussion between the internist and the ophthalmologist, the timolol was discontinued and epinephrine hydrochloride 1% and pilocarpine 1% were substituted for the timolol. The patient

bitterly objected to the constricted field caused by pilocarpine and this medication was discontinued.

Over the next 24 hours, the rate increased to between 65-75 beats per minute and the arrhythmia cleared completely. She was discharged to return to the care of her out-of-state physician.

Clinically, the patient with arteriosclerotic vascular disease had complications from two drugs—digoxin and timolol. There is ample evidence that patients with significant heart disease may not be candidates for beta blocker therapy, especially if there is evidence of defects in the conduction mechanism.

In the case presentation, even after the withdrawal of digoxin, the depression of vital signs persisted. The quick clinical response to the withdrawal of the beta blockers indicates significant systemic effects of the topically applied medications. Individuals who currently are on such drugs as propranolol have little problem with the added beta blocking effect of topically applied timolol. However in this case, negative chronotropic effects of such beta blockers significantly affected the patient whose heart was already depressed by digoxin.

Recent reports indicate that timolol has been involved in the induction of intractable asthma. This cleared only after the withdrawal of the medication. Indications for the use of these drugs were not followed. It was applied at a higher dose frequency than recommended. This case showed the potency of such medications and the potential synergy with other chronotropic agents.

Of perhaps more significance is the need for both the generalist and ophthalmologist to take a careful history with particular attention to the cardiorespiratory status of the patient. A history of glaucoma must also include the different types of medications and their frequency.

Recently at the *Colby College Course on Glaucoma*, reports of increasing frequency of the complications with timolol were reported. They have included the above mentioned problems but also feelings of depression, lassitude and worsening of angular pain in patients with otherwise compensated cardiorespiratory disease.

This case report was presented to stimulate more attention and communication among physicians concerning this new class of medication which has come into wide use.

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Conservative Treatment of Low Back Pain With Epidural Steroids

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The conservative treatment of low back pain encompasses the use of several time tested modalities.

1. Rest—to include strict bed rest—or, more simply, avoidance of strenuous pain producing activities such as bending and lifting.
2. Analgesics.
3. Lumbar flexion exercises—when pain permits.
4. Lumbar supports.
5. Anti-inflammatory agents.
6. Muscle relaxants.
7. Traction.
8. Manipulation.
9. Heat, moist or dry.

The use of the last four modalities is supported by little statistical evidence of efficacy. Their use therefore is not recommended although a brief trial is certainly not contraindicated. All methods of treatment of this common incapacitating affliction can be useful.

The mainstays of treatment then are the first five. A few comments on these are in order.

1. Rest.

Strict bed rest is by and large a practical impossibility. Very few patients will comply with this recommendation and even fewer doctors would for their own back pain. There is much anecdotal evidence but little experimental proof that strict bed rest will shorten the duration of an acute attack of low back pain. More effective means are available.

Avoidance of painful bending and lifting will be done automatically in the presence of low back pain of sufficient severity.

2. Analgesics.

These should be restricted to the use of ASA or Acetaminophen with or without Codeine which will provide sufficient relief. Potentially addicting drugs such as Oxycodone and Pentazocine are not recommended.

3. Lumbar flexion exercises.

Strengthening the abdominal musculature and decreasing thereby the lumbar lordosis is advocated by most authorities. Proper posture and lifting habits form part of the exercise program.¹

4. Lumbar support.

The cheapest, simplest form is a lumbosacral corset with posterior steel stays. It has been shown experimentally that a corset can increase intra-abdominal pressure and thus decrease intra-discal pressure. The erector spinae musculature is more active by EMG when a cor-

set is worn so there is no risk of weakening the back muscles. Some immobilization is also produced which can be beneficial in putting the painful structures at rest.

5. Anti-inflammatory agents.

There is no controversy over the use of Aspirin for low back pain. The newer non-steroidal agents are probably no more effective than Aspirin.

Oral steroids have been advocated by some for short-term use.

It would seem more appropriate to introduce the steroids where the pathology is, namely, the disc/nerve root interspace. Access to this area can be gained by an injection into the epidural space.

RATIONALE FOR THE USE OF EPIDURAL STEROIDS

The use of epidural steroids was first reported from Europe in the 50's—(Cappio²) with good results.

Goebert, et al³ reported good results in 72% of patients who had epidural steroid instillation. Brown⁴ reported better results if the injection was done within 3 months of the onset of an acute discogenic syndrome.

Dilke, et al⁵ reported on a double blind comparison of epidural steroids versus saline interspinous ligament injection and found that the steroid group did strikingly better as regards analgesic requirement and resumption of usual occupation when reviewed at three months.

Gardner⁶ and colleagues at the Cleveland Clinic reported improvement in 60% of patients receiving hydrocortisone and procaine by epidural injection.

Winnie⁷ and his colleagues at Cook County Hospital got good results with epidural steroids as well as with intrathecal steroids.

The complications reported have been mild (headache, fluid retention) and transitory in nature.

There is little doubt that inflammation in and around the nerve root is a necessary ingredient in the production of pain. Slow pressure on a peripheral nerve causes painless paresis and a shower of paresthesias as the pressure is released as will be evident to anyone who has sat too long on his sciatic nerve. Rapid pressure causes sharp transient pain and paresthesias peripherally as seen when the ulnar nerve is traumatized at the elbow.

There is evidence that a herniated nucleus pulposus or simple disc degeneration per se can initiate inflammatory changes. Gertzbein, et al⁸ found that a cellular immune response is produced in patients with sequestered discs.

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Marchal, et al⁹ presented evidence that the liberation of nuclear fluid from the healing annulus fibrosis capsule converts the glycoprotein of nuclear fluid into an antigen which results in circulating antibodies detectable in high titres 3 weeks after an acute back pain episode.

The well-known anti-inflammatory action of steroids in stabilizing lysosomal membranes therefore can be used to advantage in the treatment of discogenic back and leg pain. A higher degree of success can be obtained if the steroids are introduced around the inflamed nerve root. Easy access to the epidural space can be obtained through the sacral hiatus between the sacral cornua.

Method:

A 22 gauge 1½" needle is introduced at a 45 degree angle pointing anteriorly and cephalad between the sacral cornua penetrating the sacral membrane into the sacral canal.

Thirty cc of a mixture of normal saline and 80mg of methylprednisolone acetate (Depo-medrol®) is injected into this potential space which lies extradurally. It has been shown by the injection of contrast material that this volume is sufficient in most individuals to reach the L2-3 level at least. The procedure is done in the office without anesthesia and is somewhat painful but well accepted by the majority of patients. Reproduction of sciatica by the injection is taken as proof that the fluid has reached the desired nerve root level and occurs frequently. The patient can resume his ordinary activities after 5 or 10 minutes.

Results:

One thousand five hundred and fifty-six patients were treated for low back pain from May 1972 to May 1979. One hundred eighty-eight were lost to follow-up leaving a total of one thousand three hundred and sixty-eight with a follow-up of six months or more.

The average age was 44.3 years. The duration of symptoms was for an average of 28.2 months.

Forty-nine percent had a history of trauma.

Seventy-eight percent had roentgenographic findings of spur formation or disc narrowing.

Corset and Exercises:

The initial treatment consisted of Williams flexion exercises or the use of a lumbosacral corset with posterior steel stays.

Six hundred and sixty-two had mild functional disability and little stiffness and were treated only with exercises.

Fifty-eight percent achieved fifty percent or more pain relief either spontaneously or as a result of the treatment. The failures of treatment went on to other forms of treatment.

Six hundred and eighty-four patients were treated initially with a corset and exercises. Three hundred and twenty-eight stated that they had improved at least fifty percent in pain relief (forty-eight percent of those so treated).

Patients who failed to respond to this initial treatment or who had neurologic signs such as reflex, sensory or motor deficits and/or signs of nerve root tension; positive Lasegue, positive straight leg raising or positive bowstring sign, received epidural steroids.

Epidural Steroids:

Five hundred and nineteen patients received an average of 2.4 epidurals each at intervals of two weeks between injections.

Three hundred and seventy-eight patients (73%) were improved 50% or more. Two hundred and ninety-four of these (56.6%) obtained over 80% improvement.

Category	# Patients	% Improvement	Percentage Total
Excellent	294	80 to 100%	56.6
Good & Excellent	378	50 to 100%	73.
Good	84	50 to 80%	16.4
Failure	141		27

Those achieving less than 50% pain relief were considered as failures although in many cases the patient was pleased to get any relief at all.

Patients receiving epidural injections were those resistant cases that had little prospect of improvement. They had functional disability such as pain on bending, lifting or sitting, had not had relief by the passage of at least 3 to 6 weeks of time from the onset of symptoms or had neurologic deficits or signs of nerve root tension as explained above. The effectiveness of the injections therefore is manifest as this group was not expected to improve spontaneously.

DISCUSSION

Of the 1368 patients with 6 month follow-up, 1080 (79%) achieved more than 50% reduction in pain.

A small group—fifty-six had symptoms too mild to warrant aggressive treatment, or improved spontaneously with just the passage of time and the use of analgesics.

Of those treated with a corset and exercises alone, 48% got substantial relief.

The failures in the above group and those who could not or would not exercise or who could not or would not wear the corset or who had neurologic deficits or signs of nerve root tension, 73% were improved substantially by epidural steroids.

Some of the failures of conservative therapy went on to surgery. This represented 10% of the total number of patients.

CONCLUSIONS

1. Conservative treatment as outlined here can be expected to provide substantial relief for 79% of low back pain patients.
2. Patients with substantial disability unresponsive to the usual forms of conservative treatment can obtain relief in 73% of cases with epidural steroids.
3. Corset and exercise therapy is beneficial in 53% of patients.

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Diagnostic Imperatives in Internal Medicine

The Timely Detection of Treatable Disease

Endocrinology

MARK E. MOLITCH, M.D.*

Because most endocrine diseases are easily treated, physicians may fail to perceive them as life threatening. But the patient who goes undiagnosed is often at mortal risk, either as a direct consequence of the endocrine disorder or indirectly because of increased vulnerability to such stresses as surgery, myocardial infarction, or infection. The insidious presentation of certain endocrine diseases can be highly misleading. Addison's disease, for example, may manifest itself with fatigue, weight loss, and gastrointestinal complaints, yet if untreated may be rapidly fatal. Sometimes, a concurrent illness may draw attention away from the endocrine disorder, particularly in older patients. A common situation is that of the aged individual with coronary artery disease who develops "apathetic" or "masked" thyrotoxicosis. The patient reports only a spontaneous increase in angina, and the sole clinical findings are a resting tachycardia or the onset of atrial fibrillation. Prompt treatment of the thyrotoxicosis alleviates the angina and may interrupt its progression to myocardial infarction.

Although laboratory diagnosis of endocrine disease is usually easy, clinical recognition of the syndromes may be difficult. Therefore, a high index of suspicion is needed if diagnosis and potentially life-saving therapy are to be initiated.

THE ADRENAL CORTEX

A Life-Threatening Condition

Adrenal insufficiency (Addison's disease): Although manifestations of adrenal insufficiency may be striking once the diagnosis is suspected, initially the symptoms may be such nonspecific complaints as fatigue, weakness and lethargy. Subsequently gastrointestinal disturbance may dominate the picture; nausea, constipation alternating with diarrhea, abdominal pain, and weight loss are common. Depression with constipation, the irritable bowel syndrome or even a gastrointestinal carcinoma may be considered in the differential diagnosis. A barium enema used to evaluate such complaints can precipitate hypotension and adrenal crisis in a patient who is already volume depleted owing to adrenal insufficiency.

Sexual dysfunction is common, with loss of libido in both sexes and amenorrhea in women or im-

potence in men. Women may lose axillary and pubic hair owing to diminished production of adrenal androgens. In some patients behavioral symptoms, such as apathy and confusional states, predominate. With long-standing disease, the patient gradually becomes hyperpigmented owing to increased secretion of ACTH and lipotropin. Failure to lose a tan in the winter; darkening of new scars, palmar creases, knuckles, and areolae; and patches of dark pigmentation appearing on the buccal mucosal are all indications of Addisonian hyperpigmentation.

Adrenal insufficiency becomes life threatening when blood pressure falls to the point of hypotension with a marked postural effect. The patient is now at substantial risk of sudden death, and therapy must not be delayed. Any form of stress can plunge a relatively stable patient into shock that responds poorly to pressor agents. Unexplained hypotension in a patient should always suggest the possibility of adrenal insufficiency.

Certain typical settings increase the statistical likelihood of acute insufficiency. Spontaneous adrenal hemorrhage may occur up to 33 days following surgery; it has also been seen in patients receiving anticoagulant therapy and in those with sepsis, severe burns, or meningococcemia. Flank pain and fever are often but not always present with adrenal hemorrhage.

Routine laboratory studies in patients with adrenal insufficiency usually reveal moderate eosinophilia, hyponatremia, hyperkalemia, and azotemia.

Adrenal insufficiency can be diagnosed and primary adrenal failure can be distinguished from pituitary dysfunction through the Cortrosyn® test, which should be performed as soon as the diagnosis is suspected (Table 1). Both ACTH and cortisol levels are low in hypothalamic/pituitary disease, but in primary adrenal insufficiency ACTH is elevated. In this test, the minimum value for cortisol is 5 µg/dl, and Cortrosyn should increase the level by at least 7 µg/d and to a value of 18 µg/dl. In patients with primary adrenal disease, little or no response to Cortrosyn is seen, whereas in patients with ACTH deficiency a subnormal but definite response is usual. An abnormal result from the screening test requires confirmation with more prolonged evaluation, but when values are normal, prolonged use of steroids can be avoided.

The immediate treatment for patients with acute adrenal insufficiency consists of vigorous rehydration with normal saline containing 5 percent glucose

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TABLE 1

MANAGEMENT OF ADRENAL INSUFFICIENCY

1. Clinical Presentation: Hyperpigmentation, apathy, lethargy, weight loss, nausea, diarrhea, abdominal pain, hypotension, fever.
2. Draw blood for cortisol (serum), ACTH (heparinized on ice), and electrolytes.
3. Give dexamethasone, 4 mg, intravenously.
4. Administer Cortrosyn (synthetic ACTH) 1 ampule (0.25 μ g) intramuscularly or intravenously.
5. Draw blood for cortisol 1 hr after Cortrosyn administration.
6. Give hydrocortisone 100 mg, intramuscularly or intravenously, every 8 hours then taper.
7. Give 1-3 liters of 5 percent glucose in normal saline intravenously over the first 24 hours to correct fluid deficit.
8. If the Cortrosyn test substantiates hypoadrenalism, then further detailed testing should be carried out when patient is stable.

(D5NS). The salt is needed to restore volume and the sugar to prevent hypoglycemia. Dexamethasone is given with the cortrosyn test; after the second blood sample is obtained, additional corticoid as hydrocortisone hemisuccinate, 100 mg, is given intravenously as a bolus. This dose is repeated every eight hours until the patient's condition has stabilized. Then, over a few days, the dosage is decreased to a maintenance level.

Conditions of Major Importance

Cushing's syndrome. Cushing's syndrome results from excess secretion of cortisol by an adrenal adenoma or carcinoma, or by hyperplastic adrenal glands, or it may result from administration of exogenous steroids. Hyperplasia results from excess ACTH secretion by the pituitary or an ectopic hormone-secreting neoplasm. Although patients with Cushing's syndrome do not risk immediate catastrophe, a delayed diagnosis can result in significant morbidity: hypertension, diabetes mellitus, osteoporosis, protein breakdown with muscle weakness, and possibly peptic ulcer. When the disease is due to a pituitary tumor and the diagnosis is made early, cure can be achieved by the selective transsphenoidal resection of the adenoma. However, when the diagnosis has been missed for a prolonged period, the tumor often becomes locally invasive. When an adrenal carcinoma is responsible, the diagnosis is not usually considered in patients until the tumor is unresectable. Thus, the importance of early diagnosis cannot be overstated.

Most clinicians are familiar with the usual clinical features of Cushing's syndrome and the typical case is not difficult to diagnose. Before the syndrome is florid, however, certain features should prompt an early screening. New onset of diabetes mellitus or hypertension associated with hirsutism should arouse suspicion as should unexplained proximal myopathy and marked hypokalemia following treatment with a diuretic.

If the clinical evaluation is compatible with the diagnosis, then it should be confirmed with two laboratory screening tests. Measurement of free cortisol in a 24-hour collection of urine and the over-

night response to dexamethasone administration yield very few false negatives. In the latter test, 1 mg. of dexamethasone is given orally between 11 and 12 P.M.; at eight next morning, serum cortisol is normally less than 6 μ g/dl. Increased cortisol secretion or non-suppressibility of the hypothalamic/pituitary/adrenal axis indicates a need for further detailed testing.

Hyporeninemic hypoaldosteronism results in hyperkalemia, which can be life threatening. The disorder usually occurs in older diabetic patients who have mild renal insufficiency, and it is due to the ineffective generation of active renin by the kidney. This diagnosis should always be suspected in patients with unexplained hyperkalemia. The diagnosis is established when renin and aldosterone levels fail to rise upon diuretic-induced volume depletion of the patient. The best treatment for this disorder is a mineralocorticoid such as 9 α fludrocortisone (Florinef®) or deoxycortisone acetate (DOCA).

Hyperaldosteronism may be caused by an adrenal adenoma or by bilateral nodular hyperplasia. Patients with this disorder develop hypertension and a hypokalemic alkalosis that rarely becomes life threatening. As with Cushing's syndrome, this diagnosis should also be entertained in hypertensive patients who develop marked hypokalemia with diuretic use.

Congenital adrenal hyperplasia first appearing in adulthood is the mild type resulting from deficiency of 21-hydroxylase; there is always some degree of salt loss. This condition may lead to adrenal crisis when associated with major stress, such as surgery or infection, and thus should not be overlooked. Women usually present with complaints of virilism, and the diagnosis is established if urinary levels of 17-ketosteroids and pregnanetriol are elevated.

THE ADRENAL MEDULLA

A Life-Threatening Condition

Pheochromocytoma. Although pheochromocytoma is found in fewer than 0.1 percent of patients with hypertension, the morbidity associated with it makes early recognition important. Hypertensive crises can occur spontaneously, or they may occur at induction of anesthesia or during surgery. The characteristic clinical features of pheochromocytomas are caused by paroxysmal release of catecholamines and include headache, palpitations, sweating, fatigue and occasionally diarrhea. About 50 percent of patients have sustained hypertension instead of paroxysmal symptoms. In 5 to 10 percent of patients symptoms are very infrequent and, therefore, the first suspicion of pheochromocytoma is raised when blood pressure rises markedly during the induction of anesthesia for surgery for an unrelated disorder.

Catecholamine-secreting tumors along the sympathetic chain occur in 10 to 20 percent of patients. With these tumors paroxysmal symptoms may be provoked by particular activities; for example, swallowing if the tumor is mediastinal, micturition

when the tumor is located in the bladder wall. Occasionally recurrent abdominal pain and weight loss are seen. Rarely, the decrease in peristalsis induced by catecholamines can mimic ileus with progressive abdominal distension. Tumors secreting mainly epinephrine may produce shock when secreting and of course, hemorrhage into a tumor may also lead to shock (Manger and Gifford, 1977). Rarely, some patients even without hypertension develop congestive heart failure as a result of "catecholamine cardiomyopathy."

Diagnosis of pheochromocytomas is best approached by assaying urine for increased amounts of catecholamines and their metabolic by-products. Usually measuring vanilmandelic acid (VMA) suffices as a screening procedure, but even when VMA levels are normal, if suspicion is high metanephrine, epinephrine, and norepinephrine should be measured. It is especially useful to measure these substances during or just after an attack in a carefully timed specimen inasmuch as catecholamine levels may be normal between attacks. Provocative testing with tyramine or other agents is hazardous and rarely necessary (Manger and Gifford, 1977).

Surgical removal of a pheochromocytoma should take precedence over all other surgery except in utter emergencies. After successful resection, the patient should be evaluated for the syndrome of multiple endocrine adenomatosis Type II (Sipple's syndrome), of which pheochromocytoma may be only one manifestation. Medullary carcinoma of the thyroid should be sought with stimulation tests for calcitonin secretion. Although the carcinoma can be progressive and fatal, screening programs in kindreds with Sipple's syndrome have revealed patients with preneoplastic hyperplasia of medullary C-cells of the thyroid and the thyroidectomy has prevented the development of malignancy. Hyperparathyroidism may be an associated feature of the syndrome. Rarely, hypercalcemia is directly caused by excessive of catecholamines and disappears with adrenalectomy. In about 5 percent of patients, pheochromocytoma is associated with cutaneous neurofibromatosis (von Recklinghausen's disease) and, conversely, pheochromocytoma occurs in about 1 percent of patients with neurofibromatosis.

THE THYROID

Life-Threatening Conditions

Thyroid Storm: The diagnosis of hyperthyroidism is not usually difficult. In some patients, however, symptoms may be few and atypical, or they may simply be disregarded by the patient or physician, so that the hyperthyroidism may only be recognized when the patient is in thyroid storm. Often this state, in which mortality is 20 to 50 percent, is precipitated by an acute stress, such as surgery or infection, in an already thyrotoxic patient.

In thyroid storm, fever is invariably present and is progressive. When thyroid storm occurs postoperatively, the fever usually begins three to four hours

TABLE 2

MANAGEMENT OF THYROID STORM

1. Clinical Findings: Fever, tachycardia, restlessness, stupor, diarrhea, vomiting.
2. Laboratory Findings: Elevated T4, T3, T3 Resin Uptake, Free T4.
3. Drug Therapy
 - A. Propylthiouracil 600-800 mg, orally stat then 150-200 mg every 4 to 6 h.
 - B. ssKI, 2-5 drops, every 8 hours orally, or NaI, 0.5-1.0 g intravenously every 8 hours (starting 1-2 hours after PTU).
 - C. Dexamethasone, 2 mg, every 6 h for 4 doses.
 - D. Propranolol, 20-80 mg, every 4 hours orally or 1-10 mg intravenously every 4 hours.
 1. If severe bronchospasm give instead Reserpine 1-5 mg intramuscularly every 4 to 6 hours or Guanethidine 1 mg/kg orally every 12 hours.
 - E. If iodide toxicity can use Lithium Carbonate 300 mg. every 6 to 8 hours—checking lithium levels before each dose.
 - F. Phenobarbital 30-60 mg every 6 to 8 hours.
4. Supportive Therapy
 - A. Fluids
 - B. Calories
 - C. Oxygen
 - D. Vitamins—B-Complex, Thiamine, Vitamin C
 - E. Antipyretic—cooling blanket, iced gavage, aspirin (acetaminophen)
 - F. Digitalis if necessary
5. Treat Any Underlying Illness.

following surgery; fever starting 12 to 24 hours postoperatively is more likely due to other causes, such as atelectasis or pneumonia. A more rapid tachycardia is observed than the fever alone would warrant and atrial fibrillation with a rapid ventricular response for which digitalis is relatively ineffective may occur. Mental status may range from extreme restlessness to confusion, psychosis, seizures and coma. Severe diarrhea, nausea, vomiting, and abdominal pain may also be present.

The diagnosis of thyroid storm must be made clinically because therapy cannot be delayed for laboratory results, though obviously blood should be drawn before treatment and sent for assay of thyroxine (T4), resin uptake and triiodothyronine (T3). Then large doses of a thionamide antithyroid drug, corticosteroids, propranolol and iodides should be given along with supportive care as outlined in Table 2. A response of the therapy (largely the propranolol) should be seen within 4-6 hours and the patient should continue to improve over the ensuing hours and days. Unless the precipitating event is obvious, the cause of the episode, presumably an associated illness, should be sought.

Myxedema coma: Myxedema coma usually develops in a patient with previously undiagnosed, chronic hypothyroidism. Cold exposure, sedation, infection, hypoxia, surgery, or CO₂ narcosis may plunge the patient into coma. Clinical features suggesting myxedema coma include hypothermia, bradycardia, delayed return or absence of deep tendon reflexes, impaired consciousness, periorbital edema, coarse dry skin, alopecia, and occasionally a goiter or a thyroidectomy scar. Appropriate blood

TABLE 3

MANAGEMENT OF MYXEDEMA COMA

1. Clinical Findings: Hypothermia, bradycardia, obtundation, (thyroidectomy scar, exophthalmos, occasionally).
2. Laboratory Findings: Low T₄, T₃ Resin Uptake, T₃, Free T₄, Elevated TSH (unless hypopituitary). Frequently: low pO₂, high pCO₂, low Na, low glucose.
3. Hormone Therapy.
 - A. L-thyroxine 500 µg intravenously stat then 50 µg intravenously daily.
 - B. Hydrocortisone 100 mg intravenously every 8 hours.
4. Supportive Therapy.
 - A. Correction of hypoxia and hypercapnia
Intubation and mechanical ventilation if necessary.
 - B. Correction of Hypoglycemia.
 - C. Correction of Hyponatremia (if 120 mEq/L with 3% NaCl and furosemide).
 - D. Correction of Hypotension with colloid.
 - E. Treatment of any underlying infection.
 - F. Nasogastric suction.
 - G. Bladder catheterization.
 - H. Avoid rapid warming.
 - I. Avoid pressors if possible.
 - J. Pericardiocentesis if signs of tamponade.

tests should be performed to evaluate the possibilities of hyponatremia, hypoglycemia, hypoxia, and hypercapnea. Blood should be obtained for thyroid function tests including levels of T₄, thyroid-stimulating hormone (TSH), and free T₄ although therapy must proceed before the results can be known.

Definitive treatment consists of replacing thyroid hormone, correct metabolic abnormalities, and giving general supportive care (see Table 3). Large doses of L-thyroxine must be used to treat myxedema coma, whereas in most cases of hypothyroidism small doses are given initially and then gradually increased. The first dose of L-thyroxine is 500 µg given intravenously and then 50 µg daily. Concurrently, hydrocortisone, 100mg, should be given intravenously every 8 hours. Even with the appropriate therapy, the mortality in myxedema coma approaches 20 percent (Werner and Ingbar, 1978), but in most patients some clinical improvement is usually seen in 6 to 12 hours after therapy is begun.

Conditions of Major Importance

Hyperthyroidism: Even in the patient who does not develop thyroid storm undiagnosed hyperthyroidism can be a major source of morbidity as patients suffer from a markedly catabolic state manifested as cardiomyopathy, osteoporosis, and proximal myopathy.

Although its usual clinical features are nervousness, weight loss, hair loss, smooth skin, excessive perspiration, and heat intolerance, other findings may be more prominent. Particularly in older patients hyperthyroidism may be "masked," and the patient may appear "apathetic." In such patients there may be evidence only of weight loss or of cardiac disease such as angina pectoris or atrial fibrillation poorly responsive to digitalis. Within the last

Continued on Page 89

Quinamm™

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATIONS: For the prevention and treatment of nocturnal recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis, and static foot deformities.

CONTRAINDICATIONS: Because of the quinine content, Quinamm is contraindicated in women of childbearing potential, in pregnancy, in patients with known quinine sensitivity, and in patients with glucose-6-phosphate dehydrogenase deficiency. Hemolysis (with the potential for hemolytic anemia) has been associated with a G-6-PD deficiency in patients taking quinine.

PRECAUTIONS: Thrombocytopenic purpura may follow the administration of quinine in highly sensitive patients. Recovery will follow withdrawal of the medication. Cinchona alkaloids, including quinine, have the potential to depress the hepatic enzyme system that synthesizes the vitamin K-dependent factors. The resulting hypoprothrombinemic effect may enhance the action of warfarin and other oral anticoagulants.

ADVERSE REACTIONS: Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. If ringing in the ears, deafness, skin rash, or visual disturbances occur, the drug should be discontinued.

DOSAGE AND ADMINISTRATION:

1 tablet upon retiring. When necessary, 1 additional tablet may be taken following the evening meal.

Product Information as of September, 1977

U.S. Patent 2,985,558

Merrell

MERRELL-NATIONAL LABORATORIES Inc.
Cayey, Puerto Rico 00633

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year, we have seen two such patients admitted for coronary angiography and consideration for coronary artery bypass grafting because of refractory, progressive angina; both became asymptomatic once their "apathetic" thyrotoxicosis was treated. Other uncommon features of hyperthyroidism include hypercalcemia (20 percent), a microcytic anemia (25-30 percent), pernicious anemia (3 percent), splenomegaly and lymphadenopathy (5-10 percent), diarrhea, nausea, and vomiting. Occasionally hyperthyroidism is precipitated in individuals with goiter by administration of an iodinated contrast medium used in radiologic procedures.

One-quarter to one-half of hyperthyroid patients treated with thionamide antithyroid drugs may go into remission after 1 to 2 years; the rest require definitive long-term therapy with radioactive iodine or surgery.

Hypothyroidism: Hypothyroid patients usually present with symptoms of cold intolerance, fatigue, dry skin, coarse hair, increased sleeping, constipation, and modest weight gain. Examination reveals mental slowing, a hoarse voice, and periorbital edema. Myocardial contractility is impaired in hypothyroidism; bradycardia and pericardial effusions are often found, and respiratory function may be impaired. The hypoxic ventilatory drive is depressed in most hypothyroid patients, but the hypercapnic drive is only occasionally depressed; thus, respiratory failure, is seen only in the most severely hypothyroid patients. Because drug metabolism is slowed in hypothyroidism, any sedating drug must be used cautiously and in small doses.

The severely hypothyroid patient may suffer impaired consciousness for a variety of reasons: excessive sedation, depressed respiration causing hypercapnea and hypoxia, decreased cardiac output, and hyponatremia secondary to a defect in renal free-water clearance.

Hypothyroidism is treated with L-thyroxine, initially in doses of 25 to 50 μ g daily, then increasing over several weeks to a final daily dose between 100 and 200 μ g. Therapy with L-thyroxine alone results in a proper balance of T4 and T3; desiccated thyroid or pharmacologic combinations of T4 and T3 should not be used because they produce excessive and occasionally harmful levels of T3.

THE PITUITARY

A Life-Threatening Condition

Hypopituitarism: Unrecognized hypopituitarism may lead to rapid death under some circumstances. Most dangerous is adrenal insufficiency owing to loss of the ACTH-adrenal axis. As with primary adrenal insufficiency, vascular collapse and death may ensue, either spontaneously or in the face of stress. Hypothyroidism resulting from loss of the thyrotropin (TSH)-thyroid axis is not an immediate hazard, but the precautions and concerns listed in the section on hypothyroidism pertain.

TABLE 4

GLUCOCORTICOID THERAPY FOR SURGERY IN ADRENAL INSUFFICIENCY

1. Hydrocortisone, 100 mg, intramuscularly the night before surgery.
2. Hydrocortisone, 100 mg, intramuscularly in a.m. on call to operating room.
3. Hydrocortisone, 100 mg, intravenously over course of surgery.
4. Hydrocortisone, 100 mg, intramuscularly or intravenously evening after surgery.
5. Postoperative Day (POD) 1: hydrocortisone, 50 to 100 mg,* intramuscularly or intravenously every 8 hours.
6. POD 2: hydrocortisone, 25-50 mg, intramuscularly or intravenously every 8 hours.
7. POD 3: hydrocortisone 25 mg, intramuscularly, intravenously or orally every 12 hours; fludrocortisone (Florinef®), 0.1 mg, daily orally.
8. POD 4: hydrocortisone, 20 mg in a.m., 10 mg in p.m. orally; fludrocortisone, 0.05-0.1 mg, daily.

*For major procedures, unstable course or supervening infection the higher figures should be used with slower tapering.

Most commonly, partial hypopituitarism develops insidiously as a result of vascular insufficiency. Diabetes, postpartum hemorrhage (Sheehan's syndrome), or a tumor compressing the normal pituitary or interrupting the hypothalamic-pituitary portal vessels are the main causes. In the diabetic patient, the first sign of pituitary insufficiency may be hypoglycemia resulting from the loss of ACTH and growth hormone. In the postpartum state, the mother usually fails to lactate or resume normal menses. Pituitary tumors may present with signs of growth hormone, ACTH or prolactin excess (i.e., acromegaly, Cushing's disease or galactorrhea/amenorrhea/impotence) or signs of mass effect of the tumor, such as headache, visual field disturbance, or hypothalamic dysfunction.

Hypopituitarism may, of course, be manifested by signs that the glands controlled by the pituitary are failing to produce adequate amounts of their hormones. In addition to adrenal insufficiency and hypothyroidism, gonadal failure is the principal consequence, with loss of libido, impotence and amenorrhea. The symptoms of hypoglycemia are an unusual feature of the disease.

Skull films and tomography of the sella are usually normal in hypopituitarism. When the sella is seen to be enlarged, one of the following states should be suspected: a tumor compressing normal tissue, the "empty" sella syndrome, or infarction of a tumor. Any patient in whom an enlarged sella is found should be completely evaluated for evidence of hypopituitarism.

Occasionally hypopituitarism may appear explosively in the form of pituitary apoplexy. This condition is typified by severe headache proceeding rapidly to vascular collapse. Skull films generally show an enlarged sella, indicating tumor, and CSF is bloody or xanthochromic. Steroid administration is essential in this situation, and transsphenoidal

decompression may be necessary.

Any patient suspected of hypopituitarism should be evaluated with measurements of thyroid (T4, T3, and TSH) and adrenal (cortisol, ACTH) function. Stimulation testing to evaluate the hormonal reserve of the pituitary should be carried out after the initial screening is completed.

The principal need for hypopituitary patients is for steroid coverage to protect them during stressful events, including diagnostic procedures. After a complete evaluation, full hormonal replacement can be given as required (see Table 4).

Conditions of Major Importance

Diabetes Insipidus: Diabetes insipidus (DI) may be classified as central or nephrogenic. In central DI insufficient vasopressin (antidiuretic hormone, ADH) is produced, whereas nephrogenic DI results from the kidney's resistance to the action of ADH. Although most cases of central DI are idiopathic, many are caused by such lesions of the hypothalamus and pituitary stalk as craniopharyngioma, sarcoid granuloma, eosinophilic granuloma, or vascular infarction. Nephrogenic DI may be inherited but may also be drug-induced; lithium carbonate, demeclocycline (Declomycin®), and the anesthetic agent methoxyflurane (Penthrane®) are known to cause the disorder. Although hypercalcemia, hypokalemia, and sickle-cell anemia may produce mild concentrating defects, it is unusual for them to cause symptoms.

Both varieties of DI produce polyuria and polydipsia. In these patients, serum osmolality is elevated and urine osmolality is inappropriately low for the state of dehydration. Occasionally there may be some diagnostic difficulty in separating these disorders from psychogenic polydipsia. An overnight dehydration test usually suffices to establish the diagnosis (for details see Miller, et al, 1970). Although many patients with DI do well for years simply by increasing their water intake, prevention of life-threatening dehydration under stressful circumstances is an important goal of management. A very hot environment, an infection leading to high fever, debility or altered consciousness limiting intake of water, or suspension of oral fluids while in the hospital for diagnostic x-ray procedures may produce severe dehydration. Similarly, in a postoperative patient who develops DI, a delay of a few hours in matching fluid input to a markedly increased output can result in severe dehydration.

Central DI is controlled by administering vasopressin or the new synthetic analog of vasopressin, dDAVP. If it is suspected that the DI will last only 1 or 2 days then input fluid can simply be matched to output. Mild DI can occasionally be managed by oral agents (such as chlorpropamide, clofibrate, or carbamazepine) which either increase ADH secretion or increase the kidney's sensitivity to ADH, but most cases require vasopressin or dDAVP.

Syndrome of Inappropriate Antidiuretic Hormone

TABLE 5

ETIOLOGIES OF HYPERCALCEMIA

Common

Hyperparathyroidism
Malignancies (solid) with osseous metastases
Malignancies (solid) without osseous metastases
 Secreting parathormone
 Secreting PGE₂
 Secreting ?
Hyperthyroidism
Thiazide diuretics
Multiple myeloma
Vitamin D toxicity
Estrogen (androgen) therapy of breast cancer

Uncommon

Sarcoidosis
Diuretic phase of acute tubular necrosis
Immobilization (in adolescents and in patients with Paget's Disease)
Addison's Disease
Myxedema
Vitamin A toxicity
Leukemia/Lymphoma
Other granulomatous diseases (tuberculosis, coccidioidomycosis, Berylliosis, blastomycosis)
Milk-Alkali Syndrome
Idiopathic (associated with supraaortic stenosis in childhood)

Secretion: In this syndrome, ADH is secreted to excess either by the posterior pituitary or ectopically by a neoplasm. Patients present with symptoms of water intoxication: consciousness is impaired in a progression from confusion to coma, and seizures may occur. Patients usually appear well hydrated, and the skin and subcutaneous tissues may have a doughy feel.

Marked hyponatremia and hypochloremia are found, though hypertriglyceridemia and hyperglycemia, which may also cause hyponatremia must be excluded. Urine specific gravity is high and the marked serum hypoosmolality is accompanied by inappropriately high urine osmolality. Mild states are treated by restricting intake of free water. Severe states, with marked CNS symptoms, should be more aggressively managed by the administration of 3 percent saline and furosemide, which produces a diuresis of dilute urine.

DISORDERS OF CALCIUM, MAGNESIUM AND PHOSPHORUS METABOLISM

A Life-Threatening Disorder

Hypercalcemia: Hypercalcemia is a common laboratory finding, one present in 0.1-0.6 percent of the population. A careful investigation of hypercalcemia should always be conducted. The great majority of patients are found to have hyperparathyroidism (Table 5); however, hypercalcemia may serve as an early sign of neoplasms secreting parathyroid hormone-like substances, prostaglandins, or, in the case of myeloma, other calcium-mobilizing factors.

Severe hypercalcemia is life threatening. Pro-

gressive hypercalcemia produces altered states of consciousness ranging from an inability to concentrate through confusion, psychosis, and even coma. Severe hypercalcemia (serum calcium > 15 mg/dl) should be aggressively treated to bring the serum calcium below 12 mg/dl. The first step in therapy is rehydration with saline until a diuresis of about 200 cc. per hour is achieved. Urine losses of potassium, magnesium and sodium must be replaced intravenously. Serum calcium may have to be lowered by other means if rehydration plus diuresis is ineffective; furosemide along with saline, mithramycin, glucocorticosteroids, phosphate, calcitonin, or indomethacin are standard measures.

Conditions of Major Importance

Hypocalcemia: Hypocalcemia is usually due to hypoparathyroidism (usually induced by surgery) or vitamin D deficiency. Severe, acute hypocalcemia such as occurs after thyroid and parathyroid surgery can produce cramping, carpopedal spasm, tetany, anxiety, agitation, delirium, and seizures. Untreated hypocalcemia leads to mental deterioration, Parkinson-like rigidity, and choreiform movements. Therapy consists of replacement with calcium and vitamin D.

Hypophosphatemia: Severe hypophosphatemia can result from alcoholism, insulin therapy of diabetic ketoacidosis, prolonged antacid use, total parenteral nutrition, or postoperative fluid replacement with just dextrose and saline. Severe hypophosphatemia can give rise to altered erythrocyte metabolism; deficits in ATP and 2,3-diphosphoglycerate (2,3-DPG) decrease the ability of hemoglobin to release oxygen to tissues. Other sequelae include: hemolytic anemia; severe muscle weakness occasionally resulting in respiratory failure; and a metabolic encephalopathy consisting of irritability, paresthesias, dysarthria, confusion, seizures, stupor, and coma. Although oral phosphate preparations are usually successful for mild hypophosphatemia, severe hypophosphatemia requires parenteral therapy.

Magnesium Deficiency: Magnesium depletion can occur even while the measured serum magnesium level remains normal; therefore, when serum magnesium is found to be low, marked depletion has already occurred. Magnesium depletion is caused by alcoholism, diabetic ketoacidosis, congestive heart failure, diuretic usage, malabsorption, and prolonged parenteral fluid therapy. Clinical manifestations include lethargy, weakness, tremors, athetoid movements, cramping, mental irritability, seizures, stupor, coma, and atrial and ventricular tachyarrhythmias. When severe CNS symptoms or cardiac irritability can be attributed to magnesium depletion, therapy with magnesium sulfate should be initiated; 10 ml of a 10 percent solution is given intravenously over 15 minutes or intramuscularly followed by 1g intramuscularly every 4 or 6 hours, with frequent measurement of magnesium levels to avoid hypermagnesemia.

THE PANCREAS

Life-Threatening Disorders

Hypoglycemia: The symptoms of hypoglycemia are well known and include perspiration, tachycardia, headache, and CNS symptoms ranging from anxiety to coma. In the adult, there are four principal situations associated with hypoglycemia.

1) Most commonly it results from an overdose of insulin or is produced by one of the oral sulfonylurea drugs, especially chlorpropamide. When insulin administration is the cause, glucose ingestion suffices for mild cases of hypoglycemia, but parenteral glucagon or 50 percent dextrose given intravenously may be necessary for severe cases. Hypoglycemia caused by oral agents may be prolonged and may recur after glucose administration so all such patients should be hospitalized.

2) Reactive hypoglycemia may produce mild symptoms a few hours after a meal but is quite uncommon. Fasting hypoglycemia does not occur. This disorder rarely gives significant hypoglycemia and the patient is not in any danger.

3) Hypoglycemia associated with an insulin-secreting tumor (insulinoma) may be life-threatening either directly by causing coma and seizures or indirectly through sudden mental confusion with resultant loss of control. Both fasting and reactive hypoglycemia appear in these patients; a telltale symptom is difficulty in arousing the patient in the morning.

4) Very rarely mesotheliomas, fibrosarcomas, and other connective tissue tumors cause hypoglycemia. These tumors, like insulinomas, are treated by surgical resection and supportive therapy with glucose infusions.

Diabetic ketoacidosis: Although ketoacidosis developing in a known diabetic is usually easily recognized, ketoacidosis developing as the initial manifestation of diabetes in an adult may not be so easily recognized. However, the classical symptoms and signs are usually present; namely, polyuria, polydipsia, weight loss, polyphagia followed by nausea and vomiting, and altered levels of consciousness. Although abdominal pain and a raised serum amylase in some patients suggest pancreatitis, the amylase usually proves to be salivary in origin and the level of lipase is within normal limits. Pancreatitis is rarely a cause of diabetic ketoacidosis.

Hyperglycemic Hyperosmolar Nonketotic Coma: In this condition, the patient becomes markedly hyperglycemic and hyperosmolar without developing ketoacidosis. Lacking ketone bodies, the patient does not often develop nausea and vomiting, feels less acutely ill, and waits longer before seeking medical attention. Consequently glycosuria continues, leading to severe dehydration which, along with the hyperglycemia, results in a hyperosmolar state. In addition to severe dehydration, these patients often present with depressed consciousness and a variety of neurological signs which are usually reversible. As with ketoacidosis, this condition may prove fatal if it is not diagnosed and treated with fluids and insulin.

MULTIPLE ENDOCRINE GLAND DISORDERS

Multiple Endocrine Adenomatosis (MEA): It is important to remember that there are two autosomal dominant syndromes in which multiple glands may be affected by neoplasia. A family history of these disorders or more than one disorder found in a given patient should prompt a thorough investigation in all family members. In MEA Type I, neoplasia of the pituitary, pancreatic islets, and parathyroids may occur. In MEA II, pheochromocytomas, medullary carcinoma of the thyroid, and hyperparathyroidism may occur; occasionally gastrointestinal tract gangliomatoses accompany the other abnormalities. Therapy of both syndromes requires surgical resection of neoplastic tissue.

Multiple Endocrine Deficiencies: Autoimmune disease of the thyroid, adrenals, ovaries, parathyroids, and pituitary may occur together as well as separately and may cause deficiencies of function. These disorders may also be associated with pernicious anemia and diabetes mellitus. When a patient presents with any single autoimmune dysfunction,

it is appropriate to check these other systems if clinical findings are suggestive.

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CONSERVATIVE TREATMENT OF LOW BACK PAIN WITH EPIDURAL STEROIDS

Continued from Page 84

4. Epidural steroids injections are safe and effective and should be attempted in all cases where surgery is contemplated and can be an alternative to surgery.

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Opening for primary care physician in Portland. Regular hours 8 A.M. to 4:30 P.M.; no on-call or week-end duty. Prefer physician who is board certified, or board eligible in Internal Medicine or Family Practice. Good working environment in a general medical and dental clinic, located on Casco Bay. Facilities include in-house laboratory, x-ray, and pharmacy. U.S. Public Health Service Outpatient Clinic (207) 780-3211. Ask for Director or Chief Medical Officer.

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Experienced Family Practice/Internal Medicine/Pediatrics. Board eligible PA looking for position in solo/group practice—prefer southeastern Maine. Excellent qualifications and references. Avail. 6/80. Contact: Adele Witenstein, 2607 Welsh Rd., Apt. L-107, Philadelphia, PA 19114; Tel.: (215) 671-8546.



CONTINUING MEDICAL EDUCATION IN MAINE

Conferences and Workshops

Title: Breast Cancer Symposium
Date: March 27, 1980
Location: Maine Medical Center, Portland
Sponsor: Cancer Society, Maine Division, Research and Education Trust, and Southern Maine Radiation Therapy Institute
Credit: AMA and LCCME Category I—7 hours
Reg. Fee: To be determined
For further information contact Richard Britton, M.D., Maine Medical Center; 871-2515.

Title: Eleventh Annual Surgical Symposium on Trauma
Date: March 28, 29, 1980
Location: Maine Medical Center, Portland
Sponsors: Maine Chapter of the College of Surgeons and the Trauma Committee of the College of Surgeons
Credit: AMA and LCCME Category I—11 hours
Reg. Fee: To be determined
For further information contact Richard Britton, M.D., Maine Medical Center; 871-2515.

Title: Diabetes Update
Date: March 29, 1980
Location: A.R. Gould Memorial Hospital, Presque Isle
Sponsors: Aroostook County PSRO, A.R. Gould Memorial Hospital, and Medical Care Development
Credit: AMA and LCCME Category I—5 hours
Reg. Fee: \$10.00
For further information contact Gerald Goold, Medical Care Development; 622-7566.

Title: Aging: Old Clinical Myths and New Realities—Third Annual Robert M. True Memorial Symposium
Date: April 11, 1980
Location: Sheraton Inn, Maine Mall, South Portland
Sponsors: Mercy Hospital; Maine Medical Center, Family Practice Department; Maine Chapter, American Academy Family Practitioners; University of Southern Maine; and Area Agency on Aging
Credit: AMA and LCCME Category I and AAFP (prescribed) 8 hours
Reg. Fee: \$45 for physicians
\$25 for nurses, residents, and physician extenders
For further information contact Harold Pariser, M.D., Mercy Hospital; 774-1461.

Title: The Neurological Assessment of Childhood Behavior Disorders
Date: April 18, 1980
Location: Samoset Resort Inn, Rockport
Sponsors: Bancroft North and Medical Care Development
Credit: AMA and LCCME Category I—5 hours
Reg. Fee: \$50
For further information contact Gerald Goold, Medical Care Development; 622-7566.

Title: Maine Medical Association's Annual Scientific Session
Date: June 14, 15, 1980
Location: The Balsams, Dixville Notch, New Hampshire
Sponsor: Maine Medical Association
Credit: AMA and LCCME Category I
For further information contact Patricia Bergeron, Maine Medical Association; 622-3374.

Title: Seminar on Sports Medicine
Date: June 30—July 3, 1980
Location: Bowdoin College, Brunswick
Sponsors: Regional Medical Hospital and Bowdoin College
Credit: AMA and LCCME Category I—20 hours
Reg. Fee: Tuition \$240
For further information contact Office of Continuing Medical Education, Regional Memorial Hospital; 729-0181 Ext. 206.

Title: Tri-State Surgical Association Annual Meeting
Date: November 6-9, 1980
Location: Castle Harbor Hotel, Bermuda
Sponsor: Maine Chapter, American College of Surgeons
Credit: AMA and LCCME Category I—18 hours
Reg. Fee: To be determined
For further information contact John Towne, M.D.; 872-7713.

Programs Sponsored By Mid-Maine Medical Center/Colby College

Title: Obstetrics and Gynecology
Date: July 7-11, 1980
Credit: AMA and LCCME Category I; AAFP—18 hours
Title: Pediatrics
Date: July 14-18, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—16 hours

Title: Surgical Techniques
Date: July 15-18, 1980
Credit: AMA and LCCME Category I—16 hours
Title: Dermatology for the Non-Dermatologist
Date: July 24-28, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—16 hours

Title: Neurosurgical Techniques
Date: July 27-30, 1980
Credit: AMA and LCCME Category I—21 hours

Title: Otolaryngology
Date: August 3-7, 1980
Credit: AMA and LCCME Category I—18 hours

Title: Epilepsy
Date: August 5-8, 1980
Credit: AMA and LCCME Category I; AAFP—18 hours

Title: Ophthalmology
Date: August 10-14, 1980

Credit: AMA and LCCME Category I—18 hours
 Title: **Nuclear Medicine**
 Date: August 17-21, 1980
 Credit: AMA and LCCME Category I—28 hours
 Title: **Medical and Surgical Emergencies**
 Date: August 19-22, 1980
 Credit: AMA and LCCME Category I; AAFP (prescribed)—25 hours

Title: **Forensic Science**
 Date: August 24-27, 1980
 Sponsors: In cooperation with the National Association of Medical Examiners

Credit: AMA and LCCME Category I; AAFP—24 hours
 Title: **Pulmonary Disease**
 Date: August 24-28, 1980
 Credit: AMA and LCCME Category I—21 hours

All of the Colby activities will be based at the Colby College campus in Waterville. Registration fee is to be determined. For further information contact Robert Kany, Ph.D., Colby College; 873-1131 Ext. 267/251.

Hospital Activities

Augusta General Hospital Augusta, Maine

March 25, 1980 **Pulmonary Disease**
 7:30-8:30 a.m. Peter Barlow, M.D., Dartmouth Medical School
 April 22, 1980 **Immunology**
 7:30-8:30 a.m. Ken Smith, M.D., Dartmouth Medical School
 April 29, 1980 **Carcinoma of the Cervix**
 7:30-8:30 a.m. Mary Ellen Fenn, M.D., Maine Medical Center
 These programs have been certified AMA and LCCME Category I and AAFP (prescribed). For further information contact Mrs. Nancy Favorite; 623-4711. These programs may be viewed over ITS.

Augusta Mental Health Institute Augusta, Maine

March 20, 1980 **Factitious Illness**
 10-11:30 a.m. Theodore Stern, M.D., Instructor in Psychiatry at Massachusetts General Hospital, Harvard Medical School
 1:30-3 p.m. **Headache and the Diagnosis of Tumors**
 Theodore Stern, M.D.
 March 27, 1980 **Chronic Returnees**
 10-11:30 a.m. Brian Gottlieb, M.D., Clinical Director, Admission Unit, Augusta Mental Health Institute
 April 3, 1980 **Vocational Rehabilitation**
 10-11:30 a.m. Dennis McCrory, M.D., Consultant in Rehabilitation to the State of Massachusetts
 1:30-3 p.m.
 April 17, 1980 **Medical Management of Drug Overdose**
 10-11:30 a.m. Peter Gross, M.D., Instructor in Medicine at the Massachusetts General Hospital, Harvard Medical School; Associate Chief Emergency Medical Services, Massachusetts General Hospital
 1:30-3 p.m. **Physostigmine and the Treatment of Overdoses**
 Peter Gross, M.D.

The 10-11:30 a.m. sessions are Grand Rounds; 1:30-3 p.m. sessions are Clinical Consultations. All programs have been certified AMA and LCCME Category I. For further information contact Ulrich Jacobsohn, M.D.; 622-3751 Ext. 243.

Central Maine Medical Center Lewiston, Maine

Mar. 21, 1980 **Anaerobic Infections of the Lung—Newer**

8-10 a.m.

Aspects

John Bartlett, M.D., Tufts University School of Medicine, Boston, Massachusetts

Every Thurs. Tumor Board 12-1 p.m.
 Every Fri. Medical Grand Rounds 9-10 a.m.
 4th Fri. Joint Surgical Grand Rounds 7:45-8:45 a.m.
 (Odd Months)

2nd Fri. Visiting Professorship, Boston
 Monthly University 1-3 p.m.

All activities have been certified AMA and LCCME Category I. For further information contact Carol Murrell, Central Maine Medical Center; 795-2435.

Eastern Maine Medical Center Bangor, Maine

Every Mon. EEG Conference 12-1 p.m.
 Every Mon. Surgical Service—Chief's Rounds 5-6 p.m.
 4th Mon. ENT Section Meeting 12-1 p.m.
 4th Mon. Neurosurgery Section Meetings 4-5 p.m.
 3rd Tues. Dermatology-Pathology Conference 5-6 p.m.
 3rd Tues. Dermatology Section Meeting 6-7 p.m.
 4th Tues. Pulmonary Medicine Section Meeting 8-9 a.m.
 1st Wed. Hematology/Oncology Meeting 8-9 a.m.
 Every Wed. Tumor Clinic Conference 2-5 p.m.
 Every Wed. Radiology Conference 5-6 p.m.
 (1) Ultrasound/Nuclear Medicine
 (2) Radiology Film Review
 (3) Neuroradiology
 (4) Teaching File Conference
 (5) G.I. Radiology
 1st Thurs. Ophthalmology Section Meeting 7:30-8:30 a.m.
 OB-GYN Conference 8-9 a.m.
 (1) Pathology
 (2) GYN Analysis
 (3) OB-Pediatric Combined
 (4) In-Service and Education

Every Thurs. Pediatric Grand Rounds 9-10 a.m.
 Every Thurs. Medical Service Conference 10-11 a.m.
 Every Thurs. Cardiology Conference 11 a.m.-1 p.m.
 2nd Thurs. Orthopedic Grand Rounds 7:45-8:45 a.m.
 4th Thurs. Orthopedic Service Meeting 7:30-9 a.m.
 4th Thurs. Surgical Service Death Review 7:45-8:45 a.m.
 Every Thurs. Psychiatric Service Grand Rounds 10-11 a.m.
 4th Thurs. Urology Section Conference 7:30-8:30 a.m.
 Every Fri. Neurology Grand Rounds 8-9 a.m.

Visiting Professor Program:

1st Thurs. Medical Service Visiting Professor 10 a.m.-5 p.m.
 2nd Thurs. Anesthesia Service Visiting Professor 7-8 a.m.
 3rd Thurs. OB/GYN Service Visiting Professor 10 a.m.-4 p.m.
 Saturdays Surgery Service Visiting Professor 8 a.m.-Noon
 4th Thurs. Pediatric Service Visiting Professor 10 a.m.-5 p.m.
 as scheduled Orthopedic Service Visiting Professor
 as scheduled Family Practice Visiting Professor
 as scheduled Psychiatric Service Visiting Professor
 as scheduled Radiology Service Visiting Professor

All activities have been certified AMA Category I. For further information contact James F. Lawsing, III, M.D., Coordinator, Medical Education; 947-3711 Ext. 2303.

Henrietta D. Goodall Hospital Sanford, Maine

April 17, 1980 **Management of the Unconscious Patient**
 7 p.m. Simeon Locke, M.D., Beth Israel Hospital,

Harvard Medical School, Boston,
Massachusetts

This meeting will be held at the Henrietta D. Goodall Hospital's Conference Room. This program has been certified AMA and LCCME Category I and AAFP (prescribed). For further information contact Melvin Bacon, M.D.; 324-3632.

**Maine Medical Center
Portland, Maine**

Every Mon.	Student Technologist Conference	8 a.m.
Every Mon.	Hematology-Pathology Conference	11 a.m.
Every Mon.	Pulmonary Conference	12 Noon
Every Mon.	Pediatric Residents' Conference	1 p.m.
Every Mon.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Mon.	Surgical Pathology Review	4 p.m.
Every Mon.	Radiology Journal Club	5 p.m.
1st &	Clinical Nephrology Conference	11 a.m.
3rd Mon.		
1st &	Hematology-Pathology Conference	12 Noon
3rd Mon.		
3rd Mon.	Eye Conference	11:45 a.m.
Every Tues.	Radiology Residents' Seminar	7 a.m.
Every Tues.	Family Practice Grand Rounds	9 a.m.
Every Tues.	Electrocardiographic Interpretation	1 p.m.
Every Tues.	Psychiatric Grand Rounds	1:30 p.m.
Every Tues.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Tues.	Surgical Seminar	4 p.m.
Every Tues.	Pathology Slide Seminar	4 p.m.
1st &	Radiology-Pathology Conference	12 Noon
3rd Tues.		
1st &	Neurology Conference	12 Noon
4th Tues.		
2nd Tues.	Infectious Disease Conference	12 Noon
3rd Tues.	Hematology Conference	12 Noon
5th Tues.	Oncology Conference	12 Noon
Every Wed.	Radiation Therapy Conference	7 a.m.
Every Wed.	Urology Conference	7 a.m.
Every Wed.	Student Technologist Conference	8 a.m.
Every Wed.	Continuing Education Seminar	8 a.m.
Every Wed.	Medical Conference	9 a.m.
Every Wed.	Psychiatric Journal Club	12 Noon
Every Wed.	Cardiology Seminar	12 Noon
Every Wed.	Surgical Grand Rounds	5 p.m.
2nd Wed.	Guest Internist—Medical Conference	9 a.m.
4th Wed.	Medical Mortality Conference	9 a.m.
Alt. Wed.	Neurology-Psychiatry Seminar	11 a.m.
Alt. Wed.	Anesthesiology Journal Club	3 p.m.
Every Thurs.	Thoracic Surgery Conference	7 a.m.
Every Thurs.	OB/GYN Conference	7 a.m.
Every Thurs.	Anesthesiology Clinical Conference	7 a.m.
Every Thurs.	Diagnostic Radiology Teaching Conference	7 a.m.
Every Thurs.	Surgical Conference	8 a.m.
Every Thurs.	Pediatric Conference	9 a.m.
Every Thurs.	Tumor Consultation Board	11 a.m.
Every Thurs.	Medical Residents' Conference	12 Noon
Every Thurs.	Surgical Seminar	4 p.m.
Every Thurs.	Endocrinology Conference	5 p.m.
Every Thurs.	Dental Specialty Lecture	6 p.m.
1st Thurs.	Anesthesia Mortality Conference	7 a.m.
1st Thurs.	Guest Pediatrician	9 a.m.
1st Thurs.	Gastroenterology Conference	12 Noon
1st &	Cardiac-Surgical Conference	12:30 p.m.
3rd Thurs.		
1st, 3rd, &	Pulmonary-Physiology Conference	12:30 p.m.

5th Thurs.		
2nd Thurs.	Cardiology Teaching Conference	12:30 p.m.
2nd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
2nd Thurs.	Eye Staff Scientific Session	5:30 p.m.
2nd Thurs.	Maine Medical Center Medical Staff Meeting and Scientific Session	6 p.m.
2nd &	Pulmonary-Pathology Conference	12 Noon
4th Thurs.		
2nd &	Endocrinology Conference	12 Noon
4th Thurs.		
3rd Thurs.	Combined Guest Physician or Guest Surgeon Program	8 a.m.
3rd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
4th Thurs.	Surgical Mortality Conference	8 a.m.
4th Thurs.	Anesthesia Mortality Conference	3:30 p.m.
Last Thurs.	Pediatric Mortality Conference	9 a.m.
Every Fri.	Thoracic-Surgical Conference	7 a.m.
Every Fri.	Nuclear Medicine Conference	7 a.m.
Every Fri.	Student Technologist Conference	8 a.m.
Every Fri.	Neurological-Neurosurgical Conference	8:30 a.m.
Every Fri.	Gastroenterology Conference	9 a.m.
Every Fri.	Medical Rehabilitation Staff Conf.	9 a.m.
Every Fri.	Orthopedic Conference	9 a.m.
1st Fri.	Dermatology Conference	12 Noon
2nd Fri.	Nephrology Conference	12 Noon
3rd Fri.	Rheumatology Conference	12 Noon
4th Fri.	Oncology Conference	12 Noon
Alt. Fri.	Oncology Radiation Conference	7 a.m.
Alt. Fri.	Gastroenterology Conference	10 a.m.
All programs have been certified AMA Category I. For further information contact Costas T. Lambrew, M.D.; 871-2111.		

**Mercy Hospital
Portland, Maine**

April 3, 1980
7 p.m.

Update on the Management of Medical and Surgical Infections—The Newer Antimicrobial Agents

James Pennington, M.D., Assistant Professor of Medicine, Peter Bent Brigham Hospital

This program will be held in the Mercy Hospital Auditorium and has been certified AMA and LCCME Category I. For further information contact Gwen Gray, Mercy Hospital; 774-1461 Ext. 364.

**Mid-Maine Medical Center
Waterville, Maine**

March 20, 1980
12-1 p.m.

Cancer Chemotherapy—Oat Cell Carcinoma and Melanoma

Larry Nathanson, M.D., Tufts University School of Medicine, Boston, Massachusetts

March 27, 1980
12-1 p.m.

Case Presentation

Family Practice Residents

These programs are being held at Mid-Maine Medical Center in the South Wing Conference Room and have been certified AMA and LCCME Category I and AAFP (elective). These programs may be viewed over ITS. For further information contact David R. Ginder, M.D.; 873-0621.

**Mount Desert Island Hospital
Bar Harbor**

Every Friday
11:30 a.m.-1 p.m.

Medical Grand Rounds

This program has been certified AMA and LCCME Category I. For further information contact Christopher R. Brigham, M.D.; 288-5024.

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Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported, should these occur, discontinue drug. Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long-term therapy.

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County Society Notes

Androscoggin

The meeting of the Androscoggin County Medical Association was held on September 20, 1979 at Chase Hall, Bates College in Lewiston. The meeting was called to order at 7:20 p.m. by the President, Dr. Lawrence A. Nadeau and the program was then turned over to Dr. Leo Cousineau.

The first guest speaker for the evening was Mr. Richard Petrie, Special Investigator for the Medicaid Fraud Control Unit (Office of the Maine Attorney General). Mr. Petrie gave a brief presentation and then answered questions from members assembled.

The minutes of the June 21, 1979 meeting were distributed and a motion was made by Dr. Andre Marcotte and seconded by Dr. Thomas Shields that they be accepted as presented. This motion was passed.

A review of recent applications for membership to the A.C.M.A. was presented by the President, Dr. Nadeau. Dr. Ethan Flaks was voted to active membership as was Dr. Richard Corbin, in transfer from the Cincinnati Academy of Medicine and the Ohio Medical Association. The new Family Practice Residents were applying for junior membership; all were unanimously voted to membership following a motion by Dr. Fakhery, seconded by Dr. Marcotte.

This was followed by an introduction, by Dr. Edward Walworth, of the new Assistant Secretary. Mrs. Monique Ouellette will be taking over the duties of Miss Juliette Giguere who has resigned.

Next on the agenda was an announcement made by Dr. Candace Walworth. She briefly explained the Androscoggin Blood Pressure Control Program which is to begin in the near future. With this program, 5,000 local industrial workers will be screened for hypertension.

Dr. Frederick Holler then gave a report on the Health Care Finance Committee.

At this point, several other announcements were made. Dr. Cousineau gave an update of the status of the upcoming meeting with the Androscoggin County Bar Association. This is scheduled to take place on October 25, 1979 at Bates College. The panel will consist of two physicians, two lawyers and a moderator.

Dr. E. Walworth gave an update on the status of the new office. The furnishing and moving into the office is now complete. The telephone has been installed, the number being 783-7017.

Dr. Gilbert Grimes briefly explained the Avis Worldwide Discount Program and distributed discount cards made available to members by the M.M.A.

A motion was made to write a letter of thanks to Mr. Richard Petrie for being a guest speaker. All were in favor.

Following these business issues, Dr. Cousineau introduced Mr. Frank Stred, Executive Director of the M.M.A. Mr. Stred gave an informative presentation about the new location of the M.M.A. headquarters in Augusta and about the status of the M.M.A. as a whole.

The meeting adjourned at 9:10 p.m.

The meeting of the Androscoggin County Medical Association was held on November 15, 1979 at Chase Hall, Bates College in Lewiston. The meeting was called to order by the President, Dr. Lawrence A. Nadeau at 7:30 p.m.

Minutes were distributed and a motion was made to accept these as presented. All were in favor.

Several items of correspondence were then read. These were as follows:

1. Letter from Ms. Mildram of SAD #52 re Health Education in local schools.
2. Letter from the Maine Affiliate of the American Heart Association re Hypertension Screening Pilot Program.
3. Note of thanks from Mrs. Marion Spear.

Following these, the application of Dr. Stuart Andrews was presented. Following a motion by Dr. Victor Parisien, which was seconded by Dr. Andre Marcotte, Dr. Andrews was unanimously voted to membership as a junior member.

A memorial to Dr. William Spear was read by Dr. John Carrier.

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CRAIG W. YOUNG, M.D., Presque Isle	Aroostook	1981
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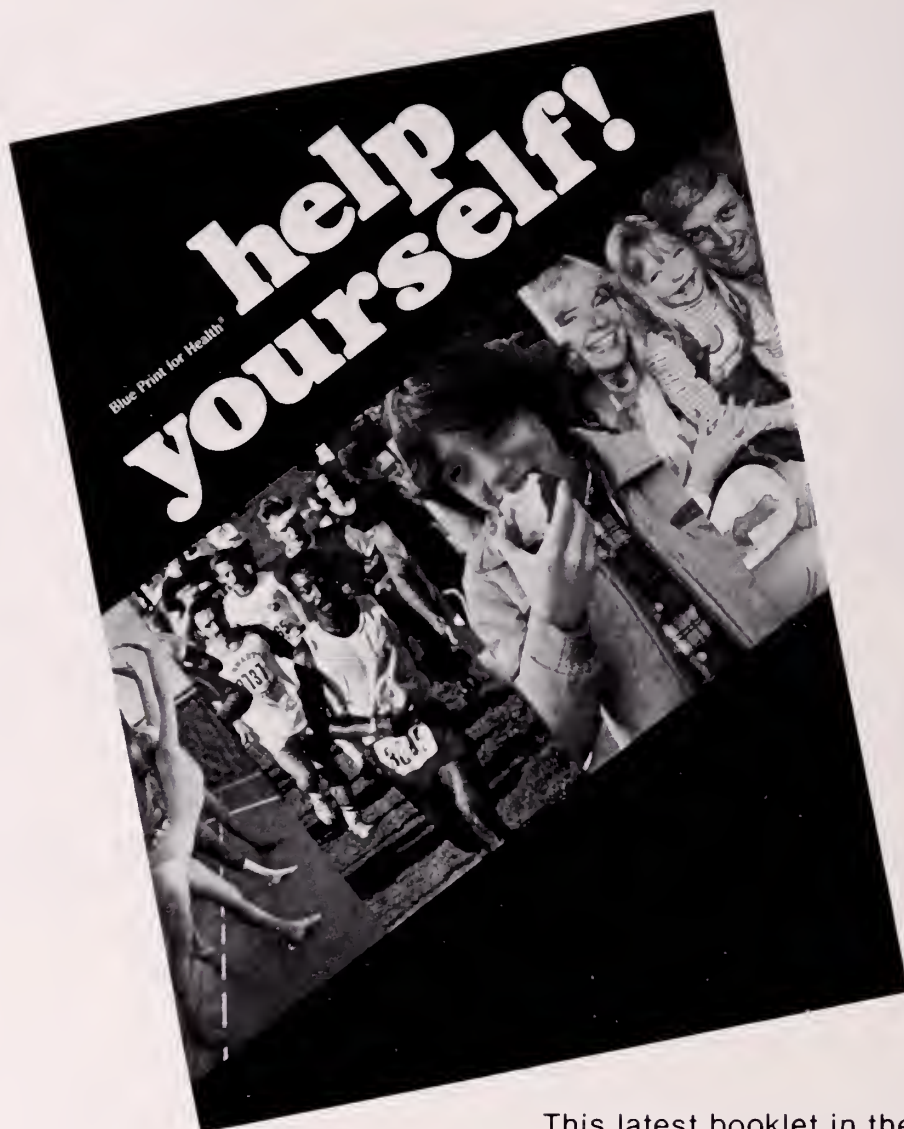
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The Psychiatric Aspects of Sports and Fitness*

BERNARD L. MACKINNON, M.D.**

My qualifications for giving this talk are: 1. I am a psychiatrist, and 2. I am an ex-athlete.

In my study I have never read much of *substance* applying psychological principles to athletic performance or applying athletic principles and experience to psychology and life. This, not because of dereliction of duty but because little of substance is written. In my practice I have only rarely treated people with problems specifically related to athletics or physical fitness.

Nonetheless, I have some thoughts on the psychiatric and psychological aspects of sports and fitness and propose to share them with you.

Before doing this, however, allow me to refer briefly to what I have read on two specific applications of exercise to emotional disorders. These are: antidepressant running and exercise as a method of reducing anxiety.

There is considerable evidence of an empiric and anecdotal nature to indicate that mild to moderate depressive symptoms can, in some people, be ameliorated or even abolished by exercise.^{1,2,3} Running is the exercise that has been most written about and the emphasis here is on comfortable running. It is important, especially in the beginning, to stay well within the adaptive limits of individuals so that they can continue to look forward to the next run. Considerations of distance, pace, and competition with others should be minimized.

Evidence for the antidepressant effectiveness of this approach is at this time not solidly established. More controlled studies are needed, but it does seem probable that the therapeutic results are at least as good, and perhaps better, than psychotherapy alone in the treatment of neurotic and reactive depression of mild to moderate degree.

As to the use of exercise to diminish anxiety, the consensus is that only vigorous exercise has a

beneficial effect.⁴ It is not known whether this is a specific effect of the exercise itself or whether diversion of energy might not be the critical factor. In this context it should be noted, for example, that T.M., biofeedback, or even simple rest in a quiet room—seem to achieve similar anti-anxiety effects.

Now back to my own reflections. I will deal with fitness first. "Mens Sana in Corpore Sano" (a sound mind in a sound body) is an ancient saying and a true ideal. But if it implies that the two frequently coexist and enhance each other then, as an idea, it is both true and false.

True, that physical exercise and physical well-being induce feelings of exhilaration, oneness-with-self, confidence, hope, and alacrity. Human beings are so constituted that fulfillment is related to use of ourselves. Mental, emotional, spiritual and physical use all bring their own gratifications. But in our sedentary age (or one that has until recently been sedentary) physical use of the self has been most neglected, and to bring to life and put into effect that which has become rusted and weak—elicits the most remarkable feelings of virtue, strength, and wholeness.

The debunking of the mind—body dichotomy is a valid debunking. Man is truly of-a-piece, of one piece. And energy, apparently, is not a pool of fixed content which can be drained in various ways, with flow in one direction depleting the supply available for flow in another. Human beings do not fit the mechanistic model. Mental expenditure exhilarates, feeds more energy into one's physical being; and physical expenditure enlivens and invigorates one's mental energy. The energy pool—within certain limits—is expandable, controlled by a feedback system—and an interlocking, interweaving, multi-stimulating and stimulated feedback system, at that.

I am ignoring in this talk the physical benefits of exercise and concentrating on psychological benefits. And when I speak of psychological benefits—refer to the mental and emotional faculties of thought, concentration, imagination, emotion, mood, will—and

*Presented at the Symposium on Sports Medicine, Bowdoin College, Brunswick, Maine on June 26, 1979.

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the expression of these faculties in behavior. I conclude that the effort and use of one's body facilitates and enhances the functioning of these mental and emotional faculties—induces a sense of competence, confidence, a sense of oneness, an overlapping of psyche and soma—toward wholeness and an enlargement of the vital force that infuses the totality of being. Undoubtedly biochemical and physiological changes are involved, but the nature of these changes is poorly understood at present.

One of the most neglected and uncomprehended psychological capacities is that of the will. The word has unscientific, even nasty overtones. You could read the ten most respected psychiatric textbooks and find no mention of "will." Much of this neglect arises from the Freudian influence which expressed and contributed to a nineteenth and twentieth century reaction against suppression and repression. Men used to be regarded as relatively autonomous creatures who bore responsibility for their faults as well as for their virtues. Personal failings and personal weakness were regarded as personal failures—or, to the extent that we were not masters of our fate, were attributed to innate deficiency or to a denial of grace. The overall implication, however, was that we bore the burden of responsibility for our own fate. "I am the master of my fate, I am the captain of my soul," said W.E. Henley in his poem "Invictus"—"The Unconquered."

"It matters not how strait the gait,
How charged with circumstance the scroll,
I am the master of my fate,
I am the captain of my soul".

But Freud changed all that. First of all, he emphasized the noxious effects of the will in the form of the harsh conscience or super ego, which denied expression to the instinctive needs and worked to suppress and repress thoughts, feelings, and actions which were contrary to social norms. The will (not a Freudian term), infusing the super ego with energy against oneself, strait-jacketed the natural self, caused inevitable conflict and stress within the self, which could erupt in the form of neurotic symptoms. I hasten to add that Freud saw much of this as an inevitable consequence of civilization, and did not himself advocate the abolition of restraint.

Freud also emphasized the unconscious. In fact it was his chief discovery, or what was called discovery, though it was more a popularization and emphasis of what had long been known. But what are the consequences of an emphasis on the unconscious? One consequence is that we are able to feel more victims than conquerors, and victims of the unknown and of the uncontrollable because it is unknown. We are not masters of our fate because we are driven by forces we neither know nor consciously influence. How then can we be responsible? We deserve neither plaudits nor blame. This belief and attitude has sunk into our culture, and influences all of us whether or not we know it.

Many of us suffer from the fear of discipline of our "natural self" and from the feeling that we are to

a large extent passive victims of fate and circumstance.

I am not attributing these deficits to Freud. He contributed, largely inadvertently, to a process—a process resulting from many complexly inter-related factors. He himself was a responsible man of iron will whose teachings have often been misconstrued and misapplied. We, nonetheless, suffer from certain consequences of his teaching by which he also would be appalled.

All positive use of self tends to counter the influences of the feelings, beliefs, and attitudes to which I have referred, and physical activity being concrete, actual, and felt—does more than most human activities to enhance the sense of power over oneself—the benefits of healthy self-discipline and the benefits of mastery and conscious self-control.

The initiation of physical action both requires the will and strengthens it; strengthens the positive use of the will in favor of oneself toward a goal; gives a sense of one's will, of one's autonomy, of one's strength. And when the action of the will in favor of oneself is felt, we revel in it—grow under its influence, expand under its power, and glow under its light.

But, as I said, there is a false side to all this too. The Greeks—athletes par excellence—preached the golden mean. Freud was right, in part, about the harshness and self-hatred, involved in the "Victorian will": the suppressing, self-hating, self-negating, humanity-crushing force of the will directed against oneself. Self-discipline and the discipline of others carried to extremes is self-hatred and other-hatred.

Freud was right too in that we are not fully free and not fully responsible. And I emphasize this because sometimes physical-fitness addicts glory too much in autonomy, and will, and discipline, and the body—become somatic facists—unhealthy minded freaks in healthy bodies. I just read an article in *Psychiatric Annals* entitled "Neurotic Illness in Fitness Fanatics"⁶ which discussed an intractable chronic neurosis developing in middle-aged males whose self-esteem was one-sidedly invested in their physical health and physical prowess.

Let me switch subjects now, or switch emphasis from the general topic of fitness to the specific topic of athletics. What do sports or athletics achieve for the individual psychologically—over and above the attributes and benefits of fitness—the sense of and the glorying in the efficiency of the body and its union with mind and, in a sense, with the world and something beyond the world.

I would enumerate the benefits as Discipline, Camaraderie, Confidence, Carelessness, Tragedy, and Joy. I could mention Courage—but while perhaps the most important of all psychological virtues—it is complex. It is neglected here but is implied in all I say. Discipline has already been discussed. So on to the rest of the list, admittedly incomplete.

Camaraderie—speaks for itself. Sport brings us into contact with others, imposes upon us the intimacy

and union with others that is required when people strive with great effort toward a common goal; impresses upon us both our differences and our commonality; makes great friends, if also—sad to say—also, at times, great enemies. Few human endeavors require this closeness—the sharing, the intensity of relationship and cooperation—and none (with the possible exception of marriage) more so than team sport.

Confidence and Carelessness—I will consider together. How many situations occur in life in which we are called upon to dig into ourselves and come up with our best of effort and of skill, and to manifest them before others—our peers, our parents, friends, and strangers. The scene and the task are recapitulated many times in life but rarely, if ever, so specifically and so intensely. If we are successful in sports and receive approval, even plaudits, it is easy to understand how this enhances our sense of confidence. If we are unsuccessful or only partially so, however, the task and the effort still confront us with the consequences of failure and humiliation—and help us to come to terms with both.

I deal with many patients who are paralyzed by risk. They dare not try for fear of failure, or they are depressed and despondent because of failure; they lack resilience in the face of failure. Athletics is the ideal arena in which to struggle—in vivo—with such issues, and to acquire the psychological attitudes which allow one not only to survive but to prevail.

We hear much of the character—building effects of athletics and I believe in this despite my knowledge of the miserable characters of many athletes. Recently Jimmy Carter, or one of his speech writers, reactivated an old motto of William James. What man needs, James said, “is the moral equivalent of war”. Never was there such a moral equivalent of war as athletic competition. Character-building, yes, for those with incipient characters; a noxious influence, perhaps, for those with physical skills which can carry them easily through, but with little innate moral fiber or character to develop.

One of my daughters recently graduated from high school and at the convocation one of the speakers twisted Socrates’ statement—“The unexamined life is not worth living” to “The over-examined life is not worth living”. He was right. As in all things, balance is required. Too much insight, prudence, intellectual intrusion, preparedness—destroy spontaneity—provide too much of a hedge against risk. In sports we are forced to take risks, to struggle toward a fine balance of striving and acceptance, toward a kind of relaxed intensity. It is a golden gift, once achieved, and athletics provide us with an opportunity to reach that balance which can carry over into life itself.

But I am talking not only about a fine carelessness but about the confidence that goes with it. Confidence is belief in oneself and acceptance of oneself. Supreme belief in one’s skills and ability to succeed is confidence, but a fragile confidence in the face of a life which, if one is honest, will ultimately undermine that belief. Acceptance of oneself, combined with

fine carelessness and resignation, and caring, and trying—melded. This is a psychological wonder; a devotion to excellence and an acceptance of failure together—a rare gift—a rare and invaluable achievement.

I recall a patient—an athlete—a good one—who was training hard, was determined to win and winning—but wasn’t sleeping, a jangle of nerves. His success was *too* important to him. His self-esteem rested too much on his prowess and his precedence. If he was to sleep and relax, he had to detach the athlete from the central self; to try hard, to strive, but also to accommodate internally to the possibility of failure.

I have dealt with many compulsive, driven, success-oriented, men—athletes of the professional and business world—who do well as long as life goes well. But they are dependent on success, lack resilience, have fragile egos, collapse when finally their effort and skill do not reap the rewards they seek. They have to learn to strive out of aspiration and a love of excellence, and full expression of self—not in defense of self or to prove self—though those are acceptable motives for young men and women who need to do some proving on the path to maturity.

This leads me to *tragedy and joy*. All of these topics are inter-related. To speak of tragedy in sport may seem to be an aggrandizement of a relatively trivial aspect of life—but I do not believe this is so. A failure to sense and confront and struggle to come to terms with the tragic sense of life is a central modern flaw. This loss is related to the loss of a broader sense of meaning and existential or, if you will, spiritual significance.

“The boast of heraldry, the pomp of pow’r,
And all that beauty, all that wealth e’er gave,
Awaits alike th’ inevitable hour;
The paths of glory lead but to the grave”.⁷

Thoughtful and sensitive athletes are confronted with the fleetingness of success and fame and with the folly involved in their pursuit. It is human to seek them. It is wise to smirk at them and at ourselves ironically.

Again, few human efforts confront us so visibly and vividly with the awareness and the task. Some successful athletes become so enamored of intensity and glory in their early years that all subsequent life is anti-climax. They cannot adjust to ordinariness, to more basic long-term goals, pursued not in the limelight but in the relative shade of day-to-day life. I recall a pathetic story from a newspaper of several years ago about a formerly famous pitcher—famous, that is, in high school, college, and the minor leagues. He never made the majors and killed himself at 31. Where? On the pitchers mound of the local ball field.

As an athlete in my younger years, I examined my own fear and realized that it was not the fear of physical hurt but the fear of hurt pride, of humiliation, of being made smaller, less significant before others and myself. Such experience and examination

Continued on Page 105

Tetanus—A Case for Maine

ALLAN M. INGRAHAM, M.D. AND AUGUST J. VALENTI, M.D.*

Tetanus, a disease known since ancient times, is still common in many parts of the world. It is regarded as uncommon in the United States where approximately 200 cases are reported yearly.¹ This dreaded affliction, associated with startling morbidity and a mortality rate that approaches 50%, is easily preventable. We record here a description of the first case of tetanus in Maine since 1972.²

REPORT OF A CASE

A 74-year-old woman fell down the cellar steps onto a dirt floor on 9-29-79. She lost consciousness for a brief time, sustained multiple contusions and a four inch laceration of the right leg below the knee. She was taken to a nearby emergency ward where her laceration was cleaned and sutured. She was sent home, but four days later she was seen at Central Maine Medical Center because of a painful jaw and back. Mild trismus and swelling over the left preauricular area were noted. The leg wound was surrounded by devitalized skin and purulent material was draining from the deeper layers. All sutures were removed. The wound was debrided and irrigated with hydrogen peroxide. Having no history of prior immunization against tetanus, she was immediately given an intramuscular injection of 250 units of Tetanus Immune Globulin (Human), TIG, and she was inoculated with adult-type tetanus toxoid (Td) at a different site.

The patient was admitted to the surgical service and given aqueous penicillin G and gentamicin intravenously. Early in her course, she complained of discomfort in her jaw, difficulty swallowing and difficulty clearing her throat.

Twelve hours after admission (4½ days post injury), she had several episodes of sudden respiratory distress and bradycardia. Shortly thereafter, she developed the generalized spasmodic activity characteristic of tetanus. Her trismus was severe by this time. The clinical diagnosis of tetanus was supported by a gram-stain of the exudate from her leg wound. It demonstrated occasional gram-positive rods and rare "tennis-racket" forms characteristic of the spore-forms. Anaerobic cultures of the wound grew *C. Tetani* in abundance.

The patient was intubated, paralyzed with pancuronium and placed on mechanical ventilatory assistance. The wound was completely excised and an additional three thousand units of TIG were administered intramuscularly. A subclavian hyperalimentation line was established; the patient was sedated and monitored in the ICU. Subsequently a tracheostomy and feeding jejunostomy were performed.

The patient became stable enough to warrant attempts at weaning her off muscle relaxants by 10-14-79. However, her blood pressure would fluctuate widely on occasion (systolic pressures ranged between 100 and 230 mm. Hg.). The pulse rate would fall precipitously and other signs of autonomic dysfunction such as profuse diaphoresis, tachycardia, and hyperpyrexia would accompany these episodes. Despite the use of antiarrhythmics such as atropine and Isuprel®, the patient expired suddenly, 14 days after her injury, during an episode of bradycardia and hypotension which lead to cardiac standstill. An EEG taken on the day of death was normal. Postmortem examination revealed no significant abnormalities other than those indicated previously.

DISCUSSION

Tetanus results from infection due to the anaerobic, spore-forming gram positive rod,

Clostridium tetani, which elaborates the neurotoxin, tetanospasmin. *C. tetani* is found in the soil and the feces of humans and animals. Low oxygen tension in contaminated wounds where necrotic tissue or a foreign body exist favors the growth of the organism. The clinical features and the management of tetanus are described in several recent reviews as well as in standard textbooks although areas of controversy persist (such as the optimum dose and route of administration of antitoxin).^{1,3,4,5} The purpose of reporting this case is to underscore the fact that tetanus immunity may be absent in the elderly patient. Although low levels of immunity in rural populations have been appreciated, recent survey of antitoxin levels in an urban adult population demonstrated that a surprising number of middle-aged women and older adults lack protective levels of antibody.⁶ Considering the availability, relative safety and effectiveness of modern tetanus toxoid preparations, it is hard to understand why so many Americans remain unprotected against this disease. Presently, those at greatest risk for developing tetanus in this country are the elderly who have not been adequately immunized and neonates.⁷

Tetanus toxoid vaccine became available prior to World War II in the United States and all servicemen were subsequently inoculated. This resulted in a considerable reduction in mortality associated with contaminated battle wounds. Antibodies to tetanospasmin, the toxin produced by *Clostridium tetani*, are developed through a series of three intramuscular inoculations with tetanus toxoid. In infants and children up to six years of age, this is included with diphtheria and pertussis immunizations (DPT) but older children and adults without a history of primary immunization should receive adult-type tetanus toxoid (Td).^{2,8} The first two injections (Td) may be given four to six weeks apart. The third is given after six to twelve months. Boosters are recommended at ten year intervals or at five years when prophylaxis for grossly contaminated wounds is considered. Over-inoculation with tetanus toxoid should be avoided as this may lead to an increase in adverse reactions.⁹

Passive immunization with antitoxin derived from horse serum has been largely replaced by immunization with Tetanus Immune Globulin of human origin (TIG). This preparation is preferred for patients without a history of immunization where prophylaxis is indicated.^{1,2,5} In these patients, 250 to 500 units of TIG should be given intramuscularly at a site distant from the site of toxoid inoculation. It may be beneficial to infiltrate the wound with part of the dose of TIG. Concomitant administration of toxoid and antitoxin does not appear to interfere with the development of antibodies.¹⁰ Antenatal immuniza-

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tion of nonimmune expectant mothers will prevent neonatal tetanus.¹¹ Natural immunity is not conferred by the disease due to the potency of tetanospasmin which is extremely toxic even in nonimmunogenic quantities. Therefore, survivors of tetanus should complete the series of toxoid injections.⁵

Despite advances in preventing tetanus through immunization, proper wound care remains the most important preventative measure. Adequate debridement, drainage and judgment regarding closure are critical steps toward reducing the risk of tetanus in contaminated wounds. Antibiotics (especially penicillin) are effective against *Clostridium tetani* although they have little effect once clinical tetanus is established.¹²

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THE PSYCHIATRIC ASPECTS OF SPORTS AND FITNESS—Continued from Page 103

force a confrontation not only with self but with values; force one to ask what really matters; help one to define and to put into perspective striving, success, fear, and failure.

And now to joy. Once we are free of fear from whatever source—we are free then to revel in the joy of effort toward excellence. Psychiatry and psychology have little to say about these broad, basic, and important aspects of healthy human life. Abraham Maslow has been an exception, and William James, and Gordon Allport, and Ernest Becker. A few others. Despite my reference to Maslow, I do not wish to talk here of transcendence or peak experience. The idea and the ideal, the experience itself is valid and valuable, but is in danger of being cheapened and diminished by too much focus and too many words. All those who have, at times, used themselves rhythmically and naturally and fully—who have an appreciation of excellence and of art—will know of what I speak.

I can do no better now than to close with a quote from George Bernard Shaw who, in the preface to "Man and Superman," wrote: "This is the true joy in life, the being used for a purpose recognized by yourself as a mighty one; the being thoroughly worn

out before you are thrown on the scrap heap; the being a force of Nature instead of a feverish, selfish little clod of ailments and grievances complaining that the world will not devote itself to making you happy".⁸

Without being foolish or naive, it is possible to believe that sport and the pursuit of fitness can contribute toward the achievement of the ideal as espoused by Shaw.

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What is a Psychiatrist?

PHILIP B. PHILLIPS, M.D.*

This identity problem has been a concern of the American Psychiatric Association for some time. Some people confuse psychiatrists and psychologists. Some know a psychiatrist is a medical doctor while others do not realize this. Some people think psychiatrists sit in ivory towers and "analyze" rich people, others think psychiatrists all work in state hospitals. This then is an attempt to make things clearer.

Psychiatrists may be men or they may be women. They are tall or short, fat or lean, black, white, brown or yellow, WASPs or second generation Russian or German Jews, Poles, Swedes, Italians, Greek, Filipinos or any combination thereof. Their ancestors may have been in the Social Register or in the Police Register; have come from Beacon Hill or Beale Street, Flat Bush Avenue or Coyote Junction, Big Bend, Oregon or Siloam Springs, Arkansas. They may work in private offices, in Community Mental Health Centers, in state or private psychiatric hospitals, teach in University Medical Schools, serve in the Public Health Service, the armed forces, in industry, in governmental administrative positions, in ghettos or on Park Avenue. They increased in numbers after World War II but in recent years there has been a decrease in the number of young graduate physicians specializing in psychiatry and this is the nation's misfortune.

Let's look at one particular type of psychiatrist, just for an example. We will call him "George S. Pipp, M.D." This is an acronym for Good, eclectically oriented, graduate educated (G.E.O.r.G.E.) S. (Solo) Psychiatrist in Private Practice, Medical Doctor. He is a well-trained physician with several years of specialized graduate training in mental and emotional illness who is first a competent physician and secondly a highly skilled psychotherapist capable of helping people suffering nervous and mental disorders and diseases, and last but not least, one who cares about people and takes the time to listen, to diagnose, to counsel, advise, direct, prescribe, and follow if need be for a period of years.

What does he do?

He takes a thorough and searching history covering the patient's life experiences prior to and including the current illness. He is interested in intrafamily relationships, specifically with parents, spouse and children, school and work achievements, military service, community associations, relationship to seniors and juniors in the work-a-day world, and especially how he can best help the patient he is

serving to make a happier, healthier and more successful adaptation to the world. Symptoms of poor or unsatisfactory emotional or physical health claim special emphasis. He will utilize medically oriented psychotherapy, psychoactive medication or somatic therapies in his attempts to help his patient. While he has also had some graduate training in neurology, he will in important types of physical illness refer his patient to a family practitioner when such seems necessary or to the proper specialist if required. In the area of psychiatric illness, he provides his patient the very best professional care he can offer. If hospitalization is required because of the patient's illness, he admits the patient to the Psychiatric Unit of a general hospital for treatment or if the patient or his family prefers, to a private psychiatric hospital for treatment by the staff. He will frequently provide effective psychotropic medication in an effort to alleviate the patient's discomfort or inappropriate thinking or behavior. He will obtain indicated laboratory examinations of body fluids, organ systems, and, when indicated, will secure psychological studies of thought processes and emotional reactions. Many psychiatrists because of their own medical training and experience are quite competent general physicians and will personally do many of the examinations without requiring the patient to be seen by consultants. When significant abnormalities require more specialized care, trained medical specialists will be called in for consultation to care for the patient's particular illness or condition. For example, a middle-aged lady in the hospital complaining of premenstrual tension and moderate edema might be treated medically by the psychiatrist as part of his handling of her case. Because of her concern over her health and the expense of her hospitalization, she might request that he personally do her semi-annual Pap smear. If abnormal cells are reported by the laboratory, he would then refer her to a competent gynecologist of her choice. An alcoholic patient with gastritis might require nothing more than antacids or a histamine receptor antagonist but if upper GI tract x-rays showed a beginning ulcer, a gastroenterologist would be the specialist to be consulted. Dr. Pipp is cognizant of the need to avoid excessive consultations because of increasing the patient's hospital expense. Not all headaches require expensive CAT scans, radioactive brain scans or EEG's. Not all chest pain calls for cardiac catheterization. Only those laboratory studies for which there is some real clinical indication should be ordered.

Psychiatrists are often the most trusted physicians a family has. "You know our family so much better than other doctors, would you take a look at Junior's throat and tell me if he really needs a tonsillectomy?" Or "Do you think mother should have her gallblad-

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der out? X-rays showed she has some stones but she has never had any real trouble. Her doctor wants to take out her gallbladder.” Or “My husband’s father is 74 and he has a hernia. The surgeon who saw him wants to repair it. Would you take a look at him please? I’d be so grateful for your opinion. I know that’s not your specialty but you are a doctor and I trust you!” Or, “Doctor, I think grandmother has had a little stroke. She acts differently and seems weaker in her right arm and leg. Could you come by tonight on your way home from the office and take a look at her?” Surely he will in each case. He is a physician and perhaps he can help.

Psychiatrists are fathers too, and some are mothers, and children require time and attention. There are Little League ball games, fishing trips, scout camps, hunting expeditions and water skiing and there is the great game of golf to be learned. There are tennis matches, basketball games, swimming meets and all these things have to be worked into his busy schedule, and it is a busy one!

There are hospital rounds from 7:30 a.m. to 10:00 a.m. seven days a week—histories and physicals—brief intensive psychotherapeutic sessions—laboratory reports to be studied—charts to be summarized—families to be called—nurses who often seek personal medical advice, and hospital administrators who want just a word with him. Those patients who are hospitalized are sick people who have to be in the hospital or they would be taken care of in the office as outpatients. They are people with schizophrenia, with severe psychotic depressions, with organic brain syndromes requiring constant care and medication or people with any type of mental or nervous condition that cannot be handled on an outpatient basis. Then there are office appointments from 10:00 in the morning or 10:30 until 6:00 or 7:00 in the evening, and these too are with sick people or people with severe problems needing his medical attention, psychotherapeutic skills and possible medication. Emergencies can be worked in during the few minutes he takes for a noon snack; then there are consultations at any other hospital in the city where a colleague has a patient he wants seen. And by 7:00 in the evening there is likely to be a hospital staff or division meeting, a county Medical Society meeting or a committee meeting or a Board of Trustees meeting or a lecture to be given and once in a while his wife requires an escort to a social affair.

And what does this busy man, this “psychiatrist” that people wonder who and what he is, do in the day time hours? He sees patient after patient after patient—sick people with serious problems. They may be veterans with service-connected emotional disorders trying to adjust to a fast-moving civilian society, Social Security claimants who may or may not be psychiatrically disabled, Workmen’s Compensation cases with emotional overlay, delinquent adolescents, depressed patients—young and old, sad, miserable, not sleeping or eating and seriously contemplating suicide, nervous persons manifesting various physical disorders; he knows not all diseases

are “in your head”. The patient with the tender upper right quadrant belly-pain radiating through to beneath the right shoulder, a hint of yellow in the eyes, a history of nausea and vomiting—is more likely suffering gallbladder disease than neurosis. And the middle aged man with episodic rectal blood loss and lower left quadrant pain, anorexia, and weight loss is a good candidate for a sigmoidoscopy and a barium enema because diverticulitis and lower bowel carcinoma are not the result of psychic conflict. When a psychiatrist sees a lady complaining of weakness, fatigue, dyspnea on exertion, pallor, or with a definite yellowish tint to the skin and some edema of the ankles he is concerned. If she also complains of anorexia, a sore mouth, nausea and some diarrhea, along with numbness of the hands and feet, perhaps spasticity of the muscles in the lower extremities and a slight ataxia, he is probably not dealing with a case of hysteria. He must be alert to this. After proper laboratory examinations, he finds she has a hyperchromic anemia with a low blood count and a relatively high hemoglobin. If gastric analysis shows a lack of hydrochloric acid in her stomach, he can be reasonably certain he is dealing with a case of pernicious anemia and that she should be under the care of a good internist. The psychiatrist must continue to be a good physician to his patients no matter how skillful he may be in psychotherapy or how up-to-date in psychopharmacology. He sees elderly patients with confusion and memory loss. Intelligent young people suffering a psychoneurosis may need a prolonged skillful person-to-person psychotherapeutic relationship and probably very little medication. He sees married couples who are having sexual problems and communication conflicts, and he tries to work with each individually and then with both together. He sees cases referred by local judges who want to be sure the accused is competent to stand trial. When attorneys or judges request his expert testimony in the court room he graciously rearranges his office schedule to accommodate the Court which has, with equal consideration, allowed him to be on thirty minute standby for his actual call to appear in the court room. He sees civil service and industrial employees to determine if their illnesses will really require retirement. He sees chronically ill patients who are hopefully being maintained with suppressive medications and infrequent visits. When these chronically ill people regress and have an exacerbation of their psychoses, he puts them back into the hospital. At times he sees severely depressed patients who have not responded to varied anti-depressive medications and he places them in the hospital of their choice and with their or their family’s permission, gives them a series of electroconvulsive treatments, then happily watches the suicidal drives disappear and grateful patients return to their jobs.

And what else does this psychiatrist do?

Like other physicians he gets a prodigious amount of mail consisting of magazines, papers, advertisements, requests for contributions, invitations to buy a thousand and one things, invest in wild enter-

prises, or go on safaris to any place in the world. He also gets from 10 to 20 medical journals and professional papers a month which require him, because he is an obsessive seeker of knowledge, to go through carefully to see what he *must* read if he is to keep up. Whatever else he can find time to read he puts into his brief case to take home at night to fall asleep over while trying to listen to his wife and children. And what else?

He belongs to his church and he donates generously though he doesn't attend as regularly as he would like. He belongs to civic clubs, luncheon clubs, and sometimes to a country club though his handicap creeps slowly upward. He serves on hospital committees and county Medical Society committees and task forces. He tries to keep up on PSRO and HSA, and NHI, and with whatever someone else in HEW has most recently proposed. Then the State Legislature goes into session and he drives to the Capitol to appear before legislative committees to explain carefully why some proposed bill is bad and why some other bill must pass. He tries to educate these well-meaning political men and women that mental illness is an ever present curse on mankind and that all reasonable efforts must continue to be made to provide help for those who have few other advocates. In the meantime he is serving on editorial boards of medical journals, reading papers submitted for publication and advising editors as to what is worthwhile and what is not. When his fellow members in the county Medical Society urge him to accept the Presidency of the society, he reluctantly but proudly accepts this responsibility knowing that his secretary and the society's executive secretary are going to be busy ladies the following year. When he is an elected delegate to the state Medical Association he takes off the necessary week, goes to the meeting, serves on reference committees and shares his knowledge and experience with other physicians guiding the state organization. He accepts appointment to more committees and more task forces knowing he must give of himself to organized medicine as well as to his own patients. And organized psychiatry makes its demands on his limited time but concerned conscience. When his District Branch requests his services as a Representative to the Assembly of District Branches, the national organization, he modestly accepts one more responsibility and forces into his crowded year the additional meetings in Washington where he represents his state psychiatric society. And here, too, there are more committees on which he will be asked to serve. Though his head says "no" his heart says "yes" and one more chore is accepted.

How can he?

How can he possibly assume all these many chores and still keep up a busy hospital and office practice with so many sick and disturbed patients? More and more he, like other physicians, turns to associates from other disciplines who can share the workload. He may find a highly trained graduate nurse, perhaps with a Master's degree, a psychologist with a Master's degree in Clinical Psychology, or as Dr.

Pipp was able to do—a woman with a Master's degree both in nursing and in Clinical Psychology who will make hospital rounds with him, dictate histories, assist in physical examinations, conduct group therapy sessions and serve as his shadow. In the office there is an experienced young woman who handles the business end of his practice, making appointments, handling billing, collections, bookkeeping and insurance, and another lady who functions as a medical secretary preparing the many psychiatric reports going out from his office, the correspondence, the speech preparation and assists with the insurance forms. These three ladies might be called the Professional Assistant, the Administrative Assistant and the Communications Assistant. And late some nights after too much coffee he sits alone in his den at home putting his own thoughts on paper for he has accepted invitations to speak at meetings of Mental Health Associations, at college classrooms, to high school science classes, to medical meetings or civic clubs. Sometimes he wonders when he will have time to sit and chat with his own beloved wife and family.

Now and then he anxiously looks at his checkbook to see if there is money for daughter's next semester's tuition at college or if he can raise the household budget to meet his wife's concerns about rising grocery prices and utility bills. And they wonder why washing machines break down just before Christmas or his wife's car needs a major overhaul in May just as graduation and wedding presents must go out to a host of children of friends or former patients.

And what do they call this man of all seasons . . . a "shrink." And if he should shrink from his overwhelming load who would take his place? His children, who in high school were teased by their classmates for having a father who was a "shrink," who disapproved of "pot", "hash" and "uppers" and "downers," who discouraged promiscuity and who cautioned against teenage marriages, grew up to be college men and women and then went out into their own careers. These proud, grown children, no longer the little kids that Dad got to see too little of, these former young rowdies who got into fights, tore up bicycles and motorcycles, dented fenders, got speeding tickets, now and then repeated a course in school, had holes in their pockets for money to fall through and sometimes talked back as they developed minds and viewpoints of their own . . . what do they say now? "Thank God," this psychiatrist says to himself, "these grown sons and daughters do call home and talk to their parents frequently and, from wherever they are in the world, they write wonderful letters to their appreciative parents and in so many ways show their love and pride as they proudly tell their young adult friends, "My Dad (or Mother) is a psychiatrist and a damn good citizen and I am proud as hell of him!"

And that, dear friends, is what a psychiatrist is . . . one who loves his fellowman, cares about people in distress, goes all out to do the very best he can for those emotionally disturbed people he serves and

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Clinical Pharmacy—The Emerging Role of the Hospital Pharmacist in Medical Care

CURT W. QUAP, M.S., R.Ph.*

Physicians are continually faced with the problem of predicting and evaluating the results of multiple drug therapy; this problem is further complicated by the introduction of new agents with scant information on their pharmacokinetics. Retaining the available information regarding the pharmacology and kinetics of these agents is a formidable task. Combining the knowledge of pharmacokinetics with additional information concerning adverse drug reactions and drug interactions is more than can be expected of a medical practitioner already inundated by the pressures of office practice and personal life.

Recognizing the problems faced by contemporary medical practitioners, the scope of pharmaceutical education is changing to prepare the pharmacist for a role which is becoming increasingly more necessary—this new area of pharmaceutical practice is termed "clinical pharmacy." Within the profession and in the academic world, a definition of this area of practice has developed which describes the clinical pharmacist as a practitioner who strives to assist the physician and other professionals in the prescribing of drug therapy through provision of drug information, monitoring patient responses to prescribed drug therapy and evaluating patient compliance to the dosage regimen ordered by the physician. Additionally, clinical pharmacists concern themselves with the effects of variables such as diet or organ function on the absorption, distribution, metabolism and excretion of therapeutic agents and the effects of drugs on laboratory test results and therapeutic outcomes. Other non-dispensing functions of the clinical pharmacist include patient and hospital staff education, participation with the physician in specialized areas of practice such as parenteral and enteral nutrition, involvement in clinical drug studies and drug utilization review.

Clinical pharmacy practice is becoming commonplace in the major teaching hospitals throughout the country. In this setting, pharmacists have become involved in a number of functions centering on drug therapy. In their efforts to aid physicians in patient care, clinically-involved pharmacists are participating in medical care by providing information on dosing, kinetics and adverse drug reactions. Patient therapy is reviewed on both a concurrent and retrospective basis to aid in identifying drug related problems such as drug interaction and the need for dosage adjustment as well as following trends in drug utilization to alert the medical staff to significant variations from recommended standards.

Other activities of the clinical pharmacist include drug histories taken by pharmacists on admission to determine compliance and complications resulting from non-prescription drug use and multiple drug therapy and patient education activities to help assure both compliance and understanding by the patient. Development of hospital formularies to help standardize the use of medicinal agents within the institution to reduce the use of outmoded therapy and lower costs and the development of pharmacokinetic programs to assist the physician in determining loading and maintenance dosages of certain drugs to avoid toxicity and assure adequate blood levels are other services of the clinical pharmacist.

The practice of "clinical pharmacy" is, however, seldom found in the non-teaching hospital as a separate entity. In many non-teaching hospitals, the dispensing pharmacist performs clinical functions as well as time and his abilities permit. The recognition of the benefits of the functions of the clinical pharmacist led to the development of a program to provide clinical pharmacy services in the three hospitals located in York County, Maine.

Due to the economic difficulties of hiring additional personnel in small hospitals, the York, Webber and Goodall Hospitals, in conjunction with the Massachusetts College of Pharmacy and with financial assistance from the Bingham Associates Fund, decided to employ a consultant clinical pharmacist to provide services on a shared basis. The objectives of this program are to aid the three pharmacy departments in providing a high level of clinical services by demonstrating the clinical function of the pharmacist to both medical and nursing staffs, involving the hospital pharmacists in the expansion of previously described clinical functions and participation in in-service educational activities and medical staff committees (i.e., Infection Control, Pharmacy and Therapeutics, Medical Care Evaluation).

Initial acceptance of the involvement of the pharmacist as part of the decision-making process in drug therapy was slow. The physicians gained confidence in the ability of the clinical pharmacist to provide accurate information primarily as a result of case discussions following drug therapy reviews by the pharmacist on both an incidental and consultation basis. The pharmacist works from a strong didactic background in pharmacology and kinetics while the physician has a decidedly more clinical involvement in drug therapy. When suggestions were offered by the clinical pharmacist, there was, and on occasion still is, some disagreement concerning the validity of those suggestions.

In one instance, the pharmacist suggested a change

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in antibiotic therapy based on the results of a routine culture and sensitivity report which showed that the cultured organism was resistant to the prescribed agent. The physician strongly disagreed stating that it is routine practice to not change an antibiotic when the patient shows a favorable clinical response in spite of the sensitivity report. The intent of the pharmacist was to have the patient placed on a less toxic and, possibly, more appropriate agent. While this example has a negative tone, it is this type of discussion which has, in other cases, led to acceptance of the pharmacist's suggestions because the pharmacist was able to offer additional information to the physician to aid in his prescription of drug therapy.

In another case involving the same physician, the pharmacist was able to identify an unrecognized adverse reaction to a new drug. This information allowed the physician to discontinue the offending agent rather than treat the adverse reaction as if it were a new medical problem for his patient. Drug-related iatrogenic problems are a frequent complication identified by the clinical pharmacist.

While physicians have used the pharmacist as a source of information regarding dosage strengths and availability of various drug agents, many have not utilized the pharmacist's knowledge of pharmacology as a means of guaranteeing safe and effective treatment of their patients. Pharmacy is a changing profession and today's pharmacist has a wealth of information within his grasp which he can and wants to provide. The clinical pharmacist, because he monitors the individual patient's therapy, can provide the physician with information which might favorably affect the patient's hospital course.

Although the clinical response of the patient is the final determinant, dosage guidelines for many medications ranging from digoxin to the aminoglycosides have been formulated which can aid in the avoidance of subtherapeutic or toxic drug levels. When a physician prescribes certain drugs, the

clinical pharmacist checks the patient's current clinical status, history, diagnosis, age, gender, body size and organ function (as measured by laboratory results) to verify that the dosage is correct based on current recommendations and consults with the physician if there is a significant variation from those recommendations. This role of the clinical pharmacist has helped to identify and, in some cases, prevent the occurrence of inappropriate responses to drug therapy.

As physicians have become aware of the contributions that the clinical pharmacist can make, they have approached the clinical pharmacist for his input and assistance in determining what agents might be prescribed in the correct dosage at appropriate intervals for a variety of disease states. This is, of course, not an everyday occurrence, nor does it involve all physicians, but as the clinical pharmacist interacts with each physician, the value of this aspect of pharmacy practice can be assessed.

This program has been in operation for two years and has made significant progress towards meeting its objectives. Pharmacy distribution systems have been up-graded to meet current standards, drug information services and newsletters have been established, educational programs have been presented to members of various segments of the hospital staffs and, perhaps most important, the working relationship between physicians and pharmacists has grown to the point where physicians are consulting with all the pharmacists concerning drug therapy and pharmacists are monitoring that therapy and voicing their comments and suggestions to the physicians, hopefully, to the benefit of the patient.

ACKNOWLEDGEMENT

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WHAT IS A PSYCHIATRIST?—Continued from Page 108

gives unstintingly of himself to his profession and his community. And, as age creeps up and life slows down he reflects soberly on the demanding career he chose and says to himself and his God, "I could not

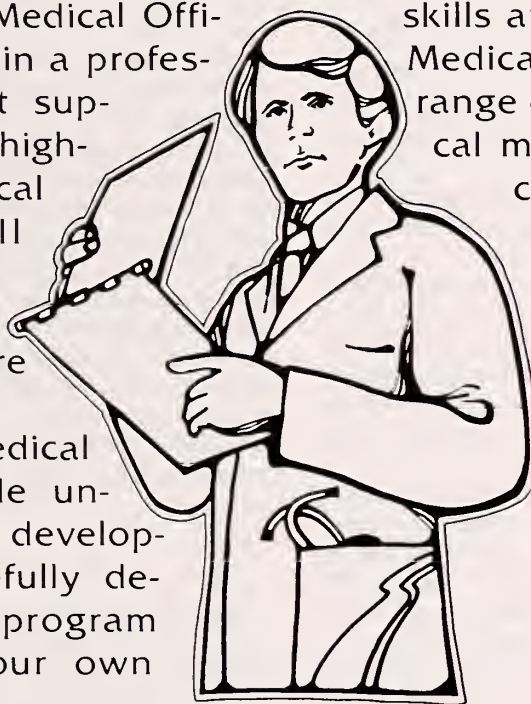
have been happy being anything else." And he bows his head humbly and admits he is a happy man!

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Prazosin (Minipress)

A Review

PAUL A. PARKER, M.D.*

Prazosin has recently been made available for marketing in the United States and represents an important addition to our current antihypertensive armamentarium.

Mechanism of Action

It produces a hypotensive effect by blocking alpha-adrenergic receptors and thereby causing peripheral vasodilatation. It thus differs in its mechanism of action from hydralazine, diazoxide, minoxidil and nitroprusside which are also vasodilators but which act to reduce the tone of vascular smooth muscles by mechanisms which are independent of direct autonomic control. Prazosin acts on the post-junctional alpha receptors and has virtually no affinity for the pre-junctional alpha receptors. This feature distinguishes Prazosin from the classic alpha-adrenoreceptor blocking agents phentolamine and phenoxybenzamine which block both the pre- and the post-junctional alpha-adrenoreceptors.¹ No central, vagal or beta-adrenergic blocking action has been shown for Prazosin as of this time.

The alpha-adrenergic action of Prazosin effects both arteries and veins. This produces a slight fall in right atrial pressure and has been shown by some investigators to reduce cardiac preload and impedance and thereby be beneficial in situations where hypertension is complicated by congestive heart failure.²

Prazosin has been shown to have no adverse effect on renal function and in fact increases creatinine clearance, glomerular filtration rate and renal plasma volume.³ Plasma renin activity, even in the presence of a diuretic, is decreased in patients treated with Prazosin but no correlation between the decrease in plasma renin activity and the degree of blood pressure lowering has ever been demonstrated.

Pharmacokinetics

Prazosin, when administered orally, is readily absorbed and this absorption is unaffected by the presence of food. Peak serum levels are attained in 2-3 hours and the half-life is approximately four hours. Greater than 94% of the drug is excreted in the form of metabolites with 90% arising from biliary secretions and being excreted via the fecal route and the remaining 10% being excreted in the urine.

Clinical Applications

Prazosin has been demonstrated to be an effective antihypertensive medication whether used as a single agent or in combination with a diuretic. Used alone it

is more effective than a diuretic alone and in combination their hypotensive actions have been found to be additive.

Clinical trials comparing prazosin's effectiveness to methyldopa and hydralazine show them to all be equally effective but hydralazine has a higher incidence of side effects than the other two drugs. The combination of prazosin with beta blockers, clonidine, methyldopa or hydralazine produces a hypotensive effect which is additive and no adverse drug interactions have been noted.⁴

Prazosin and propranolol in combinations have been found to be particularly effective. They tend to correct for the deficiencies of one another, with propranolol tending to reduce the mild standing tachycardia, tendency toward higher supine pressures and occasional increase in angina produced by prazosin and prazosin tending to block the usually unopposed alpha constriction produced by propranolol's blockage of vascular beta-2 receptors.

Prazosin has been found to be especially useful in patients with renal disease. Three advantages have been mentioned above: 1) predominant metabolism and excretion via the liver and biliary tree—thus making it safe regardless of the degree of renal failure, 2) no adverse effect on renal function, and 3) a tendency to reduce plasma renin activity. Additionally it has been found that prazosin is as effective in treating severe hypertension in patients with renal disease as it is in patients with normal renal function.⁵

Side Effects

First Dose Phenomenon

Following the administration of the first dose of prazosin, an acute syndrome characterized by orthostatically induced transient faintness, dizziness, palpitations and rarely synope has been observed. This phenomenon has been noted to occur in anywhere from 2-100 percent of patients, and factors which appear to contribute to the development of this syndrome include: 1) large starting doses (greater than 1.0 mg TID) or large increments in dose, 2) pre-existing sodium depletion, and 3) possibly the dosage formulation with tablets (not available in the United States) showing a greater tendency than capsules. The etiology of this syndrome is unclear but may be related to venodilation with pooling of blood in capacitance vessels and a selective blockage of visceral sympathetic activity leading to a redistribution of blood volume into the visceral vascular beds.

Additional Side Effects

In a small percentage of patients with pre-existing

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Diagnostic Imperatives In Internal Medicine

The Timely Detection of Treatable Disease

Dermatology

STEPHANIE PINCUS, M.D.*

Because minor disorders of skin are so common, the physician may often be lulled into discounting signs of serious skin disease or dermatologic evidence of severe systemic illness. Yet dermatologic disease can be rapidly life threatening when the barrier functions of the skin become compromised. Skin cancer, though not an immediate threat when it first appears, is most likely to be arrested by an early diagnosis. And certain systemic diseases, such as hepatitis or cancer, may first announce themselves with cutaneous manifestations.

The course of an eruption sometimes can give as much information as its appearance: the answers to certain questions can be particularly helpful. Where did the rash first appear and what did it look like? Where and how fast did it spread? Has the patient been exposed to chemicals, infection, drugs, or other potential causes in the environment? Special attention should be focused on the use of systemic or topical medications.

As the skin is examined, lesions should be classified according to standard dermatologic terminology. Particularly helpful clues can come from the distribution of a rash—for example, the characteristic pattern of photosensitivity—and the presence of sharp lines of demarcation, which suggest contact with an external agent.

DIFFUSE CUTANEOUS ERUPTION

Painful, red skin

Erythroderma is the final stage of diffuse inflammatory skin disease; it may develop in the course of days or over a much longer period. In erythroderma the skin is diffusely edematous, intensely erythematous, hot, and dry; the patient complains of pain and, on occasion, pruritus. Some degree of scaling is usual; when it is prominent the condition is termed "exfoliative erythroderma." As a rule, reddening of the skin is most conspicuous at the outset, and scaling becomes more apparent after a few days. Erythroderma is most frequently seen in patients over the age of 45 and is much more common in men than women.

By disrupting the barrier functions of the skin, erythroderma puts the patient at risk in several ways. Bacterial infection of the skin may be followed by bacteremia. Fluid loss through the damaged epidermis may lead to volume depletion and hypotension,

TABLE 1

CAUSES OF ERYTHRODERMA

Psoriasis
Drug hypersensitivity
Dermatitis
Atopic
Seborrheic
Allergic contact
Stasis with autosensitization
Lymphoma or leukemia
Pemphigus foliaceus
Pityriasis rubra pilaris

and loss of proteins can result in hypoproteinemia. Increased blood flow through the inflamed skin creates difficulties with thermoregulation and may also precipitate high-output cardiac failure.

As the disease becomes chronic, alopecia and dystrophy or even loss of the nails may occur. Lymphadenopathy is frequent even in the absence of an underlying lymphoma. Longstanding erythroderma is likely to cause hypo- or hyperpigmentation, especially in heavily pigmented people.

The term erythroderma is used to describe a particular constellation of physical findings and does not imply an etiology. In most cases, the histology is merely that of dermatitis but occasionally is suggestive of psoriasis or pemphigus foliaceus; sometimes a lymphomatous infiltrate is seen. Erythroderma has a wide variety of known causes which are listed in Table 1. An etiologic diagnosis can sometimes be made from a history of prior skin disease, drug treatment, or environmental exposure. When erythroderma develops from hypersensitivity to a drug, there may be an antecedent history of morbilliform or eczematous eruption induced by a drug. Patients with psoriasis are at risk of exfoliative erythroderma after treatment with systemic steroids. When erythroderma is accompanied with intense pruritus, atopic dermatitis or underlying lymphoma are likely etiologic factors. Unfortunately, in at least one-third of the cases no etiology can be found. Patients with erythroderma should be promptly hospitalized and treated with systemic steroids, and when there is evidence of secondary infection, antibiotics. Except in cases resulting from drug ingestion, erythroderma is often a prolonged, difficult therapeutic challenge.

Another condition which may present with tender,

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red, warm skin is *toxic epidermal necrolysis*, sometimes known as Lyell's syndrome or "scalded skin" syndrome. Marked cutaneous erythema and tenderness develop rapidly, and progress quickly to cover the entire body. Within hours the skin becomes fragile and with minimal application of pressure the superficial epidermis peels off (the Nikolsky sign). The patient then appears as if he has sustained a scalding burn of his whole body.

Though patients of all ages may develop the syndrome, etiology is usually quite different in children and adults. In young children, the disease is usually due to localized infection with staphylococcus carrying phage type 71. The phage-carrying bacteria elaborate a specific toxin which causes the generalized rash and produces a specific histologic picture of subcorneal epidermal damage. This type of toxic epidermal necrolysis is extremely rare in adults unless there is severe underlying diseases. The toxic epidermal necrolysis of adults is predominately a manifestation of hypersensitivity to a drug such as phenytoin, sulphonamides, and other antibiotics. The histologic appearance of drug-induced disease includes subepidermal blisters and overlying epidermal necrosis.

The two kinds of toxic epidermal necrolysis should be carefully distinguished because the treatment of one condition is inappropriate for the other. Antibiotics should be given for the staphylococcal variant and systemic steroids for the drug-induced condition. Indeed, antibiotics such as penicillin or its derivatives are often the cause of erythroderma. But most important in treatment is appropriate topical care similar to that given burn patients. In addition, fluid balance and intravascular volume must be carefully monitored because these patients may lose large amounts of fluid through their denuded skin.

"Blistering" Skin

The acute onset of epidermal fragility in which blisters develop or skin sloughs after slight trauma may be a manifestation of pemphigus vulgaris, a serious disease. This syndrome must be distinguished from conditions such as erythema multiforme or bullous pemphigoid, which present with extensive blistering but in which the *uninvolved skin is apparently normal* and from certain hereditary diseases, such as *epidermolysis bullosa*. Table 2 lists conditions which may cause bullous skin disease. However, only toxic epidermal necrolysis (see above) and pemphigus vulgaris among them are associated with a Nikolsky sign, the blistering or sloughing of as yet uninvolved skin when minimal pressure is applied.

Pemphigus vulgaris is a disease of old age and is associated with the appearance of antibodies to epithelium. It may begin as a florid bullous eruption with the Nikolsky sign. The blisters are flaccid, superficial, and easily broken; so the disease may present with widespread superficial, painful erosions that heal with difficulty. More frequently and less dramatically localized blisters or erosions appear

TABLE 2

SOME CAUSES OF BULLOUS DISEASE		
	Nikolsky Sign	Oral Involvement
<i>Hereditary</i>		
Epidermolysis bullosa	±	
Porphyria		
Benign familial pemphigus		
<i>Infections</i>		
Impetigo		
Viral infections—Herpes	+	
Toxic epidermal necrolysis (Staphylococcal)		
<i>Allergic</i>		
Erythema multiforme		+
Contact dermatitis		
<i>Immunologic</i>		
Pemphigus vulgaris	+	+
Bullous pemphigoid		
Dermatitis herpetiformis		
Herpes gestationis		
<i>Other</i>		
Pressure (coma or overdose of hypnotic drugs)		
Porphyria cutanea tarda		

especially in the mouth. On occasion, toxic epidermal necrolysis may initially present with fragile, blistering skin, in the absence of erythema. Both porphyria cutanea tarda and variegate porphyria may also be associated with fragile skin and localized blister formation. However, abnormalities of liver function and photosensitivity should suggest the diagnosis of porphyria.

A clinical diagnosis of pemphigus should be confirmed by histopathologic examination of a skin biopsy obtained from the edge of the lesion. A blister formed by cleft located immediately above the basal cell layer is pathognomonic. When available, immunofluorescent testing may detect the presence of circulating antibodies or antibody deposited in the skin between epidermal cells. A quick diagnosis is sometimes possible if free-floating (acantholytic) cells are noted on cytologic examination of blister fluid.

Because pemphigus has a high morbidity and was usually fatal before steroids were used to treat it, the disease should be vigorously treated with systemic steroids, immunosuppressive therapy, or gold.

Photosensitivity

Depending on its etiology, photosensitivity may vary in appearance from edema, erythema and blister formation to a more eczematous dermatitis, but in all cases it is largely or exclusively confined to sun-exposed areas. Typically the nose, cheeks, "V" of the neck, and dorsum of the hands are affected, and shaded areas, such as the upper lip and bottom of the chin, are relatively spared. Cutaneous photodermatoses can be divided into manifestations of systemic disease and those caused by an exogenous substance, either ingested or topically applied (Table 3).

The most common adverse reaction to light is

TABLE 3

COMMON CAUSES OF CUTANEOUS PHOTODERMATOSIS

Exogenous Agents	Severe overexposure (sunburn)
	Contact photosensitivity halogenated salicylanilides, furocoumarins (psoralens), sunscreens, coal tar and its derivatives
	Drug-induced photosensitivity sulfonamides, sulfonyleureas, tetracyclines and derivatives, thiazide diuretics, griseofulvin
Systemic Disease	Collagen-vascular disease discoid lupus erythematosus, systemic lupus erythematosus, dermatomyositis
	Porphyria porphyria cutanea tarda, erythropoietic protoporphyria

severe *sunburn* from overexposure. This condition is most often seen early in the summer and in fair skinned patients. Within hours painful edema and erythema appear; the peak reaction, with extensive blister formation and sometimes constitutional symptoms, occurs at approximately 48 hours. In patients with known overexposure, early treatment with systemic steroids will prevent constitutional symptoms and severe blister formation.

Systemic lupus erythematosus is frequently accompanied with a photosensitivity reaction, the morphology of which is highly variable; other than generalized photosensitivity these eruptions may include reddish-purple urticarial plaques and papules, malar erythema, oral lesions, periorbital edema, alopecia, and the discoid lesions described below. Periungual erythema and linear cuticular telangiectasias also suggest lupus, as do involvement of other organs and abnormal laboratory findings. Sun exposure may provoke the underlying disease organ systems to flare up. Photosensitivity in *discoid lupus* is highly variable, but the majority of patients do note that sunlight exacerbates their existing lesions, which are typically erythematous, well defined, scaly patches that, on healing leave atrophic, scarred skin with telangiectasias.

Most physicians are aware of the typical cutaneous findings in *dermatomyositis*: heliotrope erythema of the eyelids and face; scaly erythematous plaques over the knuckles; and periungual telangiectasias. A unique feature of the disease in many patients is the development of florid, beefy erythematous plaques after sunlight exposure. Unlike the diagnosis of lupus, which can be made by serologic and histologic findings, the diagnosis of dermatomyositis is sometimes difficult because the histology is nonspecific and muscle involvement is highly variable. Dermatomyositis should be treated early to minimize permanent cutaneous scarring and muscle damage.

In contrast to the collagen-vascular diseases, the mechanisms underlying the photosensitivity eruptions of porphyria are relatively well known. In pa-

tients with *erythropoietic protoporphyria* the elevated protoporphyrin, circulating in the cutaneous vasculature is directly responsible for the absorption of light. Patients typically develop burning and tingling in the skin immediately after light exposure and go on to develop lesions which may vary from urticarial eczematous plaques to bullae. The diagnosis is made by the detection of protoporphyrin within erythrocytes. Treatment with beta-carotene is highly effective.

In *porphyria cutanea tarda* (PCT), the offending porphyrins, uroporphyrinogen and coproporphyrinogen can be detected in the urine. PCT is frequently associated with alcoholic liver disease, elevated levels of serum iron, or estrogen use. Currently the treatment is phlebotomy to reduce hepatic stores of iron.

Photosensitivity eruptions caused by exogenous agents are usually divided into two groups: phototoxic reactions, in which the cutaneous damage is due to absorption of light by the sensitizing molecule, and photoallergic reactions, in which the sensitizing substance is modified by light and thus becomes an allergen. These reactions may occur with either systemic administration or topical application of the substance. Phototoxic eruptions can be minimized by reducing drug dosage or decreasing exposure to light. Photoallergic eruptions necessitate discontinuation of the offending agent, and are likely to recur whenever the patient is challenged and then exposed to light. Certain drugs—hydralazine, procainamide, and isoniazide—are sometimes responsible for lupus-like eruptions.

Pruritus

Pruritus of the whole body, with or without secondary excoriations, is most frequently due to primary skin disease, especially dry skin. Infestations with scabies, which are responsible for many cases, are marked by intensification at night and a characteristic distribution on the hands, in the groin, and around the waist. On rare occasions, generalized pruritus may reflect serious systemic disease. Patients with intractable pruritus, unrelieved by the usual therapeutic measures and not associated with dermatologic disorders, should be studied for systemic causes of pruritus. Potentially treatable, occult conditions of which pruritus can be an initial sign include obstructive jaundice, hypothyroidism and hyperthyroidism, lymphoma (especially Hodgkin's disease) and polycythemia vera.

LOCALIZED LESIONS

Whether conditions discussed here begin as a single lesion or multiple lesions scattered over the body, the lesions are always discrete and the intervening skin appears normal.

The formation of blisters is a common reaction pattern of skin as illustrated by a partial list of causes in Table 2. Though blisters are frequently associated with clearcut and treatable diseases such as bullous impetigo or allergic contact dermatitis, on occasion they may herald serious disease, especially when they

are associated with oral lesions, as in pemphigus vulgaris and erythema multiforme.

Erythema multiforme is a hypersensitivity reaction manifest clinically by erythematous macules or papules with central purpura (the iris or target lesion) or by erythematous vesicles and bullae. In the more severe forms, involvement of the mucous membranes is common. When mucous membranes are severely affected and constitutional symptoms appear, the disease is sometimes called Stevens-Johnson syndrome. Such severe disease may also be complicated by conjunctivitis and corneal ulceration, genital lesions, and respiratory involvement. The diagnosis is made on clinical grounds and confirmed by histologic findings of a perivascular and dermal-epidermal lymphocytic infiltrate, which frequently progresses to subepidermal blister formation. Erythema multiforme is commonly a manifestation of drug hypersensitivity and is also associated with a wide variety of infectious diseases, caused by *Mycoplasma*, herpes, *Histoplasma*, and bacteria. Patients with moderate and severe erythema multiforme require systemic steroids.

Other causes of disease in which bullae are histologically located below the epidermis are dermatitis herpetiformis and bullous pemphigoid. The clinical picture of *dermatitis herpetiformis* varies from symmetrically distributed, grouped erythematous papules to vesicles to large bullae. However, characteristically intense pruritus is a helpful clue to the diagnosis. Many patients prove to have an associated gluten-sensitive enteropathy, though it is rarely present as overt malabsorption. Dapsone® and sulfapyridine are highly effective both for relieving the symptoms and preventing the formation of new lesions.

Bullous pemphigoid, a disease of the elderly, often begins as a non-specific urticarial or eczematous disease which culminates within days to weeks with development of large, tense bullae. These tense bullae and the absence of a Nikolsky sign help distinguish pemphigoid from pemphigus vulgaris, in which the bullae are small, flaccid, and easily sloughed. Steroid treatment is usually effective.

A variety of less common diseases may also present with bullae. Herpes gestationis is an intensely pruritic vesicular eruption of pregnant women; in appearance it resembles bullous pemphigoid. Bullae on the hands, forearms, and face, as in a photosensitivity reaction, should suggest porphyria cutanea tarda or phototoxic reactions. Bullae, erosions, or synechiae of the conjunctivae and mouth, with some extension onto the adjacent skin, should suggest a diagnosis of cicatricial pemphigoid, sometimes known as benign mucous membrane pemphigoid.

Papules

The term papule defines any small (<1 cm.), circumscribed, palpable, elevated lesion produced by epidermal or dermal processes. Most conditions leading to the formation of papules require no immediate intervention; others though not common,

benefit from early diagnosis and treatment. Lesions appearing rapidly should be examined for purpura or petechiae which suggest that small blood vessels are being damaged. Petechial or purpuric papules appearing in crops suggest small-vessel (leukocytoclastic) vasculitis, an acute infectious process, meningococcemia or gonococcemia, or subacute bacterial endocarditis. Appropriate history, physical examination, and laboratory tests can be used to distinguish these possibilities. Larger subcutaneous papules and nodules are sometimes early indicators of polyarteritis nodosa, pancreatitis, or panniculitis.

Papules that grow slowly or appear over a period of weeks may imply a neoplastic process. If pigmented, they may represent melanomas; amelanotic melanomas, on the other hand would appear as reddish papules. More keratotic lesions could represent squamous cell carcinoma. These possibilities are mentioned not because they are likely to cause the development of new papules, but because early excision can significantly alter the prognosis.

Miscellaneous Lesions

Certain common conditions in exceptional circumstances signal the need for rapid or drastic intervention.

"Ordinary" urticaria usually represents a hypersensitivity reaction mediated by IgE. However, when lesions have a petechial component and persist for more than 24 hours, vasculitis should be considered and an erythrocyte sedimentation rate performed. If the sedimentation rate is increased, biopsy is the next step. On occasion, rheumatic fever or juvenile rheumatoid arthritis presents with urticaria. A patient who develops lesions on exposure to cold as when swimming should have an "ice cube test." When skin rewarms after the ice is removed, urticaria appears on the exposed skin and confirms the diagnosis of acquired cold urticaria. This diagnosis is important in that patients should be warned to avoid extensive cold exposure, which can lead to massive histamine release and hypotension.

Petechiae usually indicate vascular fragility or thrombocytopenia and are frequently accompanied by ecchymoses. Causes of *non-thrombocytopenic* purpura include scurvy, infections (with rickettsia and neisseria, for example), macroglobulinemia, and fat emboli.

Ulcers developing in unusual locations or with an active inflammatory margin may be due to vasculitis. Ulcers on the extremities and a history of purpura developing after cold exposure may indicate cryoglobulinemia.

Erythema nodosum—painful, red to purple nodules appearing on extensor surfaces, usually pretibial—may indicate tuberculosis, antecedent streptococcal infection, fungal infection (histoplasmosis, coccidioidomycosis or blastomycosis), or drug reaction. Patients with erythema nodosum should be routinely screened with tests adequate to exclude these possible etiologic factors.

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PRazosin (MINIPRESS): A REVIEW—Continued from Page 112

angina pectoris, an increase in the incidence and severity of symptoms has been noted. Other side effects have included hypotension and tachycardia with standing, headache, dry mouth, lassitude, nervous irritability, nasal congestion, fluid retention, depression, hallucinations, dreams, gastrointestinal disturbances, rash and polyarthralgia.

It is especially important to note, however, that the incidence of sexual dysfunction and failure of ejaculation is very low.

Dosage

In outpatients, the starting dose should be 1 mg orally three times per day. The patient should be advised of the first dose phenomenon and therapy should be initiated in the evening, preferably at the time of retiring. If it should be necessary to begin therapy in an office setting, it would be advisable to have the patient remain for at least two hours and observed. The dosage can be doubled after three days and if the blood pressure remains uncontrolled a beta blocker or a thiazide diuretic should be added. In resistant cases, the dosage of prazosin may be increased to a total of 20 mg per day. Once blood pressure control is established it is usually possible to

reduce the dosage frequency to twice daily with no limitation in the therapeutic effectiveness.⁶ In recumbent hospitalized patients, larger initial doses and more rapid increases in dosage may be employed.

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1. Stokes, G.S., Oates, H.F.: Prazosin: new alpha-adrenergic blocking agent in treatment of hypertension. Cardiovas. Med., 3:41-57, 1978.
2. Awan, A.N., Miller, R.R., Miller, M.P., Specht, K., Vera, Z., Mason, D.T.: Clinical pharmacological and therapeutic application of prazosin in acute and chronic refractory congestive heart failure. Amer. J. Med., 65:146-154, 1978.
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4. Stokes, G.S., Gain, J.M., Malony, J.F., Raftos, J., Stewart, J.H.: Long term use of prazosin in combination or alone for treating hypertension. Med. J. Aust. 2(Suppl): 13-16, 1977.
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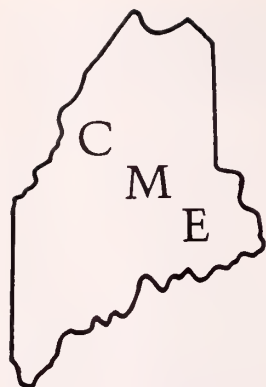
Annual Meeting Dates For Your 1980 Calendar...

Maine Medical Association, June 12-15

The Balsams, Dixville Notch, New Hampshire

American Medical Association, July 20-24

Downtown Chicago Marriott, Chicago



CONTINUING MEDICAL EDUCATION IN MAINE

Conferences and Workshops

Title: Maine Medical Association's Annual Scientific Session
Date: June 14, 15, 1980
Location: The Balsams, Dixville Notch, New Hampshire
Sponsor: Maine Medical Association
Credit: AMA and LCCME Category I
For further information contact Patricia Bergeron, Maine Medical Association; 622-3374.

Title: Seminar on Sports Medicine
Date: June 30-July 3, 1980
Location: Bowdoin College, Brunswick
Sponsors: Regional Memorial Hospital and Bowdoin College
Credit: AMA and LCCME Category I—20 hours
Reg. Fee: Tuition \$240
For further information contact Office of Continuing Medical Education, Regional Memorial Hospital; 729-0181 Ext. 206.

Title: Family Medicine Update
Date: September 8-10, 1980
Location: Spruce Point Inn, Boothbay Harbor
Sponsors: AAFP and Medical Care Development
Credit: AMA and LCCME Category I and AAFP (prescribed)—15 hours
Reg. Fee: \$150; \$120 for State of Maine AAFP members
For further information contact Gerald Goold, Medical Care Development; 622-7566.

Title: Tri-State Surgical Association Annual Meeting
Date: November 6-9, 1980
Location: Castle Harbor Hotel, Bermuda
Sponsor: Maine Chapter, American College of Surgeons
Credit: AMA and LCCME Category I—18 hours
Reg. Fee: To be determined
For further information contact John Towne, M.D.; 872-7713.

PROGRAMS SPONSORED BY MID-MAINE MEDICAL CENTER/COLBY COLLEGE

Title: Obstetrics and Gynecology
Date: July 7-11, 1980
Credit: AMA and LCCME Category I; AAFP—18 hours
Title: Pediatrics
Date: July 14-18, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—16 hours

Title: Surgical Techniques
Date: July 15-18, 1980
Credit: AMA and LCCME Category I—16 hours
Title: Dermatology for the Non-Dermatologist
Date: July 24-28, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—16 hours

Title: Neurosurgical Techniques
Date: July 27-30, 1980

Credit: AMA and LCCME Category I—21 hours
Title: Otolaryngology
Date: August 3-7, 1980
Credit: AMA and LCCME Category I—18 hours
Title: Epilepsy
Date: August 5-8, 1980
Credit: AMA and LCCME Category I; AAFP—18 hours
Title: Ophthalmology
Date: August 10-14, 1980
Credit: AMA and LCCME Category I—18 hours

Title: Nuclear Medicine
Date: August 17-21, 1980
Credit: AMA and LCCME Category I—28 hours
Title: Medical and Surgical Emergencies
Date: August 19-22, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—25 hours

Title: Forensic Science
Date: August 24-27, 1980
Sponsors: In cooperation with the National Association of Medical Examiners
Credit: AMA and LCCME Category I; AAFP—24 hours
Title: Pulmonary Disease
Date: August 24-28, 1980
Credit: AMA and LCCME Category I—21 hours

All of the Colby activities will be based at the Colby College campus in Waterville. Registration fee is to be determined. For further information contact Robert Kany, Ph.D., Colby College; 873-1131 Ext. 267/251.

Hospital Activities

Augusta General Hospital Augusta, Maine

April 22, 1980
7:30-8:30 a.m. **Immunology**
Ken Smith, M.D., Dartmouth Medical School

April 29, 1980
7:30-8:30 a.m. **Carcinoma of the Cervix**
May Ellen Fenn, M.D., Maine Medical Center

May 27, 1980
7:30-8:30 a.m. **Pediatrics—Blood Gases**
George Little, M.D., Dartmouth Medical School

These programs have been certified AMA and LCCME Category I and AAFP (prescribed). For further information contact Mrs. Nancy Favorite; 623-4711. These programs may be viewed over ITS.

Augusta Mental Health Institute Augusta, Maine

May 1, 1980
10-11:30 a.m. **Medical-Psychiatric Drug Interactions**
Jerrold G. Bernstein, M.D., Assistant Clinical Professor of Psychiatry, Harvard Medical School; Assistant Psychiatrist, Massachusetts General Hospital; Research Psychiatrist, Alcohol

and Drug Abuse Research Center, McLean Hospital; Associate Medical Director, Human Resource Institute

1:30-3 p.m.

MAO Inhibitors

Jerrold G. Bernstein, M.D.

May 8, 1980

To be announced

May 15, 1980

Hyperkinesia

10-11:30 a.m.

Michael Jellinek, M.D., Clinical Fellow in Psychiatry, Harvard Medical School; Clinical Associate in Psychiatry, Massachusetts General Hospital

1:30-3 p.m.

Organization of a Child Psychiatry Program

Michael Jellinek, M.D.

May 22, 1980

Issac Ray—Maine Physician

10-11:30 a.m.

Jacques M. Quen, M.D., Professor of Psychiatry, Department of Psychiatry School of Medicine, Cornell University, Ithaca, New York

The 10-11:30 a.m. sessions are Grand Rounds; 1:30-3 p.m. sessions are Clinical Consultations. All programs have been certified AMA and LCCME Category I. For further information contact Ulrich Jacobsohn, M.D.; 622-3751 Ext. 243.

Central Maine Medical Center Lewiston, Maine

May 21, 1980

Mid-Trimester Abortion

12 Noon

Mark Levine, M.D., Central Maine Medical Center

Every Thurs.

Tumor Board

12-1 p.m.

Every Friday

Medical Grand Rounds

9-10 a.m.

4th Friday
(Odd Months)

Joint Surgical Grand Rounds

7:45-8:45 a.m.

2nd Fridays

Visiting Professorship, Boston University

1-3 p.m.

All activities have been certified AMA and LCCME Category I. For further information contact Carol Murrell, Central Maine Medical Center; 795-2435.

Eastern Maine Medical Center Bangor, Maine

May 3, 1980

Gastroenterology

8 a.m.-12 Noon

John J. McDevitt, M.D. and Philip G. Hunter, Eastern Maine Medical Center

May 22, 1980

Visiting Professor Day in Orthopedics

10 a.m.-3 p.m.

Arthur E. Ellison, M.D., Williamstown, Massachusetts

Every Mon.

EEG Conference

12-1 p.m.

Every Mon.

Surgical Service—Chief's Rounds

5-6 p.m.

4th Mon.

ENT Section Meeting

12-1 p.m.

4th Mon.

Neurosurgery Section Meetings

4-5 p.m.

3rd Tues.

Dermatology-Pathology Conference

5-6 p.m.

3rd Tues.

Dermatology Section Meeting

6-7 p.m.

4th Tues.

Pulmonary Medicine Section Meeting

8-9 a.m.

1st Wed.

Hematology/Oncology Meeting

8-9 a.m.

Every Wed.

Tumor Clinic Conference

2-5 p.m.

Every Wed.

Radiology Conference

5-6 p.m.

(1) Ultrasound/Nuclear Medicine

(2) Radiology Film Review

(3) Neuroradiology

(4) Teaching File Conference

(5) G.I. Radiology

1st Thurs.

Ophthalmology Section Meeting

7:30-8:30 a.m.

OB-GYN Conference

8-9 a.m.

(1) Pathology

(2) GYN Analysis

(3) OB-Pediatric Combined

(4) In-Service and Education

Every Thurs.

Pediatric Grand Rounds

9-10 a.m.

Every Thurs.

Medical Service Conference

10-11 a.m.

Every Thurs.

Cardiology Conference

11 a.m.-1 p.m.

2nd Thurs.

Orthopedic Grand Rounds

7:45-8:45 a.m.

4th Thurs.

Orthopedic Service Meeting

7:30-9 a.m.

4th Thurs.

Surgical Service Death Review

7:45-8:45 a.m.

Every Thurs.

Psychiatric Service Grand Rounds

10-11 a.m.

4th Thurs.

Urology Section Conference

7:30-8:30 a.m.

Every Fri.

Neurology Grand Rounds

8-9 a.m.

Visiting Professor Program:

2nd Thurs.

Medical Service Visiting Professor

10 a.m.-5 p.m.

2nd Thurs.

Anesthesia Service Visiting Professor

7-8 a.m.

3rd Thurs.

OB/GYN Serv. Visit. Professor

10 a.m.-4 p.m.

Saturdays

Surgery Service Visiting Professor

8 a.m.-Noon

4th Thurs.

Pediatric Service Visiting Professor

10 a.m.-5 p.m.

as scheduled

Orthopedic Service Visiting Professor

as scheduled

Family Practice Visiting Professor

as scheduled

Psychiatric Service Visiting Professor

All activities have been certified AMA and LCCME Category I. For further information contact James F. Lawsing, III, M.D., Coordinator, Medical Education Committee; 947-3711 Ext. 2303.

Henrietta D. Goodall Hospital Sanford, Maine

May 20, 1980

Drug Therapy 1980

7 p.m.

Darrell R. Abernethy, M.D., Ph.D., Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

This meeting will be held at the Henrietta D. Goodall Hospital's Conference Room. This program has been certified AMA and LCCME Category I and AAFP (prescribed). For further information contact Melvin Bacon, M.D.; 324-3632.

A. R. Gould Memorial Hospital Presque Isle, Maine

April 28, 1980

Pacemaker Therapy

7 p.m.

William S. Wilson, M.D., Eastern Maine Medical Center

May 5, 1980

Hyperlipidemias

7 p.m.

Leonard J. Levy, M.D., Eastern Maine Medical Center

May 12, 1980

Subject to be announced

7 p.m.

Paul Minton, M.D., Maine Medical Center

May 19, 1980

Amyloidosis

7 p.m.

Keith McAdam, M.D., Tufts University School of Medicine

These meetings will be held at the Rotary Regional Educational Center at the A.R. Gould Memorial Hospital. These programs have been certified AMA and LCCME Category I. For further information contact Marilyn Dean; 769-2511.

Maine Medical Center Portland, Maine

Every Mon.

Student Technologist Conference

8 a.m.

Every Mon.

Hematology-Pathology Conference

11 a.m.

Every Mon.

Pulmonary Conference

12 Noon

Every Mon.

Pediatric Residents' Conference

1 p.m.

Every Mon.

Anesthesia Formal Resident Lecture

3:30 p.m.

Every Mon.

Surgical Pathology Review

4 p.m.

Every Mon.	Radiology Journal Club	5 p.m.	4th Thurs.	Surgical Mortality Conference	8 a.m.
1st & 3rd Mon.	Clinical Nephrology Conference	11 a.m.	4th Thurs.	Anesthesia Mortality Conference	3:30 p.m.
1st & 3rd Mon.	Hematology-Pathology Conference	12 Noon	Last Thurs.	Pediatric Mortality Conference	9 a.m.
3rd Mon.	Eye Conference	11:45 a.m.	Every Fri.	Thoracic-Surgical Conference	7 a.m.
Every Tues.	Radiology Residents' Seminar	7 a.m.	Every Fri.	Nuclear Medicine Conference	7 a.m.
Every Tues.	Family Practice Grand Rounds	9 a.m.	Every Fri.	Student Technologist Conference	8 a.m.
Every Tues.	Electrocardiographic Interpretation	1 p.m.	Every Fri.	Neurological-Neurosurgical Conference	8:30 a.m.
Every Tues.	Psychiatric Grand Rounds	1:30 p.m.	Every Fri.	Gastroenterology Conference	9 a.m.
Every Tues.	Anesthesia Formal Resident Lecture	3:30 p.m.	Every Fri.	Medical Rehabilitation Staff Conf.	9 a.m.
Every Tues.	Surgical Seminar	4 p.m.	Every Fri.	Orthopedic Conference	9 a.m.
Every Tues.	Pathology Slide Seminar	4 p.m.	1st Fri.	Dermatology Conference	12 Noon
1st & 3rd Tues.	Radiology-Pathology Conference	12 Noon	2nd Fri.	Nephrology Conference	12 Noon
1st & 4th Tues.	Neurology Conference	12 Noon	3rd Fri.	Rheumatology Conference	12 Noon
2nd Tues.	Infectious Disease Conference	12 Noon	4th Fri.	Oncology Conference	12 Noon
3rd Tues.	Hematology Conference	12 Noon	Alt. Fri.	Oncology Radiation Conference	7 a.m.
5th Tues.	Oncology Conference	12 Noon	Alt. Fri.	Gastroenterology Conference	10 a.m.
Every Wed.	Radiation Therapy Conference	7 a.m.	All programs have been certified AMA Category I. For further information contact Costas T. Lambrew, M.D.; 871-2111		
Every Wed.	Urology Conference	7 a.m.	Penobscot Bay Medical Center Rockland, Maine		
Every Wed.	Student Technologist Conference	8 a.m.	May 9, 1980	The Brain—Neurotransmitter Substances	
Every Wed.	Continuing Education Seminar	8 a.m.	11 a.m.-2 p.m.	Ivor Jackson, M.D., Associate Professor of Medicine, Tufts University School of Medicine	
Every Wed.	Medical Conference	9 a.m.	This program has been certified AMA and LCCME Category I. For further information contact Lloyd Roberts, M.D.; 594-9511.		
Every Wed.	Psychiatric Journal Club	12 Noon	V. A. Hospital Togus, Maine		
Every Wed.	Cardiology Seminar	12 Noon	April 21, 1980	General Medical Staff Meeting	
Every Wed.	Surgical Grand Rounds	5 p.m.	2-3 p.m.	Presentation by Assistant Chief of Staff	
2nd Wed.	Guest Internist—Medical Conference	9 a.m.	May 5, 1980	General Medical Staff Meeting	
4th Wed.	Medical Mortality Conference	9 a.m.	2-3 p.m.	Presentation by Psychiatry/Psychology	
Alt. Wed.	Neurology-Psychiatry Seminar	11 a.m.	May 13, 1980	General Medical Staff Meeting	
Alt. Wed.	Anesthesiology Journal Club	3 p.m.	12-1 p.m.	Presentation by Medical Service	
Every Thurs.	Thoracic Surgery Conference	7 a.m.	May 16, 1980	ITS presentation	
Every Thurs.	OB/GYN Conference	7 a.m.	11-12 Noon	Neurology Lecture—Historical Perspectives on Huntington's Disease	
Every Thurs.	Anesthesiology Clinical Conference	7 a.m.	Donald Osterburg, M.D., Assistant Professor, Neurology, B.U.S.M. and Assistant Chief, Neurology, BVAOPC		
Every Thurs.	Diagnostic Radiology Teaching Conf.	7 a.m.	May be viewed over ITS		
Every Thurs.	Surgical Conference	8 a.m.	Every Wed.	Medical Staff Service Meetings	
Every Thurs.	Pediatric Conference	9 a.m.	1:15-2:15 p.m.	1:15-2:15 p.m.	
Every Thurs.	Tumor Consultation Board	11 a.m.	Every other Thurs.	Oncology Clinic	
Every Thurs.	Medical Residents' Conference	12 Noon	2-3 p.m.	2-3 p.m.	
Every Thurs.	Surgical Seminar	4 p.m.	2nd Tues. of month	Psychiatric CME Meetings	
Every Thurs.	Endocrinology Conference	5 p.m.	May 7, 1980	Pulmonary Rounds	
Every Thurs.	Dental Specialty Lecture	6 p.m.	12-1 p.m.	Brinton Darlington, M.D., Augusta General Hospital	
1st Thurs.	Anesthesia Mortality Conference	7 a.m.	ITS Presentation		
1st Thurs.	Guest Pediatrician	9 a.m.	These activities have been certified AMA and LCCME Category I. No registration fee. For further information contact E. Osborne Coates, Jr., M.D., VAM and ROC, Togus; 623-8411		
1st Thurs.	Gastroenterology Conference	12 Noon	ANNOUNCEMENT: Medical Care Development, Inc. is now receiving a listing of continuing medical education activities taking place in Vermont, New Hampshire, and Massachusetts. If you wish further information contact Gerald Goold, Medical Care Development; 622-7566		
1st, 3rd Thurs.	Cardiac-Surgical Conference	12:30 p.m.			
1st, 3rd, & 5th Thurs.	Pulmonary-Physiology Conference	12:30 p.m.			
2nd Thurs.	Cardiology Teaching Conference	12:30 p.m.			
2nd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.			
2nd Thurs.	Eye Staff Scientific Session	5:30 p.m.			
2nd Thurs.	Maine Medical Center Medical Staff Meeting and Scientific Session	6 p.m.			
2nd & 4th Thurs.	Pulmonary-Pathology Conference	12 Noon			
2nd & 4th Thurs.	Endocrinology Conference	12 Noon			
3rd Thurs.	Combined Guest Physician or Guest Surgeon Program	8 a.m.			
3rd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.			

ANNOUNCEMENT: Medical Care Development, Inc. is now receiving a listing of continuing medical education activities taking place in Vermont, New Hampshire, and Massachusetts. If you wish further information contact Gerald Gould, Medical Care Development; 622-7566.

A motion was made, seconded and passed that a copy of this resolution be sent to Dr. Spear's family and that a copy be made part of the permanent records of the A.C.M.A.

Dr. Nadeau then announced that the Association is seeking new representatives to the PSR-PTO. Any interested member is asked to contact Dr. Nadeau as soon as possible.

Dr. Frederick Holler then summarized the proposed agenda for the November 17, 1979 meeting of the House of Delegates.

The meeting adjourned at 8:45 p.m.

EDWARD Z. WALWORTH, M.D., *Secretary*

Lincoln-Sagadahoc

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges Inn in Wiscasset on November 20, 1979.

There were twenty-eight members and guests present. The meeting was called to order at 8:20 p.m. by President Cote; the secretary read the October minutes, which were accepted as read.

There was no old business; there were no committee reports.

Dr. Alan W. Zeller, for several years a junior member of this Society, is back in the State of Maine, as medical director of the Bath Iron Works. He discussed the problem of industrial accident treatment and asked that physicians notify BIW of any injuries allegedly suffered at BIW.

Dr. Bostwick then introduced Mr. Frank Stred, Executive Director of the M.M.A., and Dr. Brinton Darlington, its President. They spoke on the challenges facing M.M.A. during the 1980's.

The Lincoln-Sagadahoc County Medical Society held its regular meeting at The Ledges in Wiscasset on December 18, 1979. Twenty-nine members and guests were present.

The President, Dr. P. Richard Cote called the meeting to order; the minutes of the November meeting were accepted as read by the Secretary. There was no old or new business.

The report of the Nominating Committee was accepted unanimously without additions or changes. The results of the Annual Election were:

President: Dr. Frank O. Avantaggio, Jr., Damariscotta

Vice-President: Dr. David W. Schall, Brunswick

Secretary-Treasurer: Dr. Richard C. Leck, Bath

Delegates to the M.M.A. House of Delegates: Drs. Robert H.

Dixon, Bath, Richard Evans, III and Gerry S. Hayes, both of

Brunswick. Alternate Delegates: Drs. Douglas G. Long,

Boothbay Harbor, Everett D. Schubert, Damariscotta and

John C. Skillings, Brunswick

M.M.A. Executive Committee Nominee: Dr. Louis Bachrach, Brunswick

Censors: Drs. Avantaggio, Carl R. Griffin, Jr., Boothbay Harbor and Daniel H. Wood, Bath

Program Committee: Drs. Wood and John S. Van Orden, Brunswick

Committee on Health Care Financing: Dr. Bachrach

Dr. Van Orden then gave an illustrated discussion of Orthopedic Emergencies.

GEORGE W. BOSTWICK, M.D., *Secretary*

Kennebec

The Kennebec County Medical Association met at the Silent Woman Restaurant in Waterville on December 20, 1979, with approximately 120 members and guests in attendance.

The application of Dr. John Baker was read; the remainder of the meeting was devoted to an entertaining presentation by the noted humorist, Marshall Dodge.

The meeting was adjourned with no further ado.

The Kennebec County Medical Association met at the Holiday Inn in Augusta on January 17, 1980. There were 41 members and one guest in attendance representing an excellent turnout since only three members from Waterville came down because of the freezing drizzle. Following a very pleasant cocktail hour and roast beef dinner, the Vice President, Dr. Robert Stram called the meeting to

order in the absence of the President, Dr. John Towne.

The minutes of the previous meeting were accepted without being read. A letter from Dr. Kenneth Smith to the Maine Medical Association was read resulting in the vote of the members to extend to Dr. Smith an affiliate membership.

Under old business, the application of Dr. John Baker was favorably acted upon and Dr. Baker was elected to membership.

New business:

Dr. Feagin presented suggested changes to the Constitution and Bylaws which had been discussed by the Council. The thrust of these is to add the Maine Medical Executive Committee Members and a representative of the medical staff of each hospital in the County to the Council. After some discussion, it was decided that it should be the Chief of Staff of each hospital or his designate so that the Chief of Staff could come and see us if they wished, or if they were not members or had other duties, they could designate another person to serve in that role. These changes require a vote to amend the Constitution and Bylaws and can be acted upon at the next meeting.

Election of delegates to the house: Drs. Moore, Towne, Stram, Gareth Jones, Pepe, Neil Newton and Earle Davis were elected as delegates. Drs. Dow, Shaw, Culver, Milliken, Leadley, Gould and Szucs were elected as alternates.

The Council motion "that the interest on the savings of the Association be spent in support of health care scholarship to be awarded to graduating seniors at Kennebec County High Schools" was accepted with condition that this be referred to a Committee for further deliberation prior to implementation.

Dr. Stram then introduced Mr. Frank Stred who presented a very interesting analysis of the current activities of the Maine Medical Association which was received with great interest by members present.

The meeting was then adjourned.

O. THOMAS FEAGIN, M.D., *Secretary*

Knox

The Knox County Medical Society met at the Sail Loft Restaurant in Rockport on January 8, 1980 at 6:30 p.m. Twenty-two members were in attendance. Invited guest was Dr. Jeremy Morton. After dinner, a short business meeting was held. At the business meeting, Dr. Bernard Mann was elected by the Society to affiliate membership to the Maine Medical Association. The AMA principles of medical ethics and position paper on Chiropractic was presented. No discussion ensued. Membership applications of Dr. Gary Russell and Dr. Robert Phelps were presented for vote by the Society and approved.

Following this, Dr. Jeremy Morton and his staff presented an update on the Medical Mutual Insurance Company of Maine and a lively discussion with specific interests toward managing malpractice risk in current medical practice. Very informative and interesting discussion ensued.

Additional business was then conducted and the Knox County Medical Society voted and approved the nominating committee's selection of Dr. Corwin Olds as President, Dr. Mustafa Onat as Vice-President, and Dr. Albert J. Lantinen as Secretary-Treasurer. Dr. Albert J. Lantinen will be elected a member to the executive committee of the Maine Medical Association. Delegates to the M.M.A. will be Drs. Peter Shrier, Judy Anderson and Lloyd Roberts. Alternate delegates will be Drs. John Cox, Olaf Anderson and John Williams.

There being no further business, the meeting was adjourned at 10:00 p.m.

ALBERT J. LANTINEN, M.D., *Secretary*

Washington

A regular meeting of the Washington County Medical Society was held in the Staff Library at the Down East Community Hospital on January 22, 1980, with 12 members and guests present.

The meeting opened at 7:20 p.m. under the direction of Dr. James C. Bates, President of the Society.

Minutes of the last meeting, read and approved.

Dr. Bates introduced Dr. Peter J. Leadley, head of the State P.S.R.O. organization. Dr. Leadley covered many aspects of relationship between P.S.R.O. hospitals and physicians. He covered an agreement which was made between the Associated Hospital Service of Maine and the Pine Tree Organization for Professional Standard Review; also on the ongoing medical care evaluation study of Emergency Room Organization, which will cover the many aspects of ER use. He also covered a memorandum of Understanding for Professional Peer Review Services for ambulatory care review between the Pine Tree Organization for Professional Standard Review, Inc. and the Maine Dept. of Human Services. Dr. Leadley's informative discussion brought forth many questions from the doctors present. Dr. Leadley said that 95% of his time was spent with activities relating to P.S.R.O.

A motion was made by Dr. Donald M. Robertson that it be brought to the attention of the Dept. of Human Services of the over-utilization of patients on Medicaid for doctors' services and that Medicaid patients be made aware of this fact. This was seconded and passed.

Dr. Bates then introduced Dr. Brinton T. Darlington of Augusta, Maine, President of the Maine Medical Association.

Dr. Darlington stated that cost containment is of major importance. He stated that only so much money is being made available to the State for Medicaid costs and that a major part of this was being paid to Nursing Homes which is a fairly fixed figure. The amount available to the State is more liable to be reduced, than increased, particularly during the next two (2) years and it is therefore very important that each individual physician work towards reducing the cost per patient.

Dr. Darlington also stated it is very important that physicians get to know their local Legislators and also to get to know bills that are important to the Medical Association, so that he can talk knowledgeably to the Legislator about these bills. The Medical Association will attempt to inform members of the contents of various impending bills.

Dr. Darlington also stated that The Journal is costing the Association money and they are looking into this, but due to its importance, they will make every effort to keep it going.

The name of Dr. F. James Whalen of Machias, Maine was brought up for admission to the Washington County Medical Society. It was moved, seconded and passed that he be admitted to membership.

Dr. Robert G. MacBride of Lubec, Maine is Delegate to the Maine Medical Association and Dr. F. James Whalen of Machias, Maine was elected as Alternate Delegate to the Maine Medical Association.

Dr. Donald G. Robertson of Harrington, Maine, Delegate to the Executive Committee from Washington and Hancock Counties brought up matters presented at the Executive Committee meeting which he stated meets almost monthly.

Dr. Robertson stated that the Association originally owned property in Augusta and planned to build there. Due to the resignation of Dr. Daniel Hanley, the Executive Director and loss of the quarters in Bowdoin College, it was necessary to make a move. The Association found that it would be extremely expensive to build a new building. Therefore, they looked for an alternative plan and found a building on the outskirts of Augusta that would suit their needs. This building was purchased and remodeled and will apparently fill the needs of the Association for some time to come. It also has a meeting room for the Executive Committee.

Dr. Robertson stated that there had been considerable change in relationship to Blue Cross and Blue Shield. They will maintain a continuing relationship with Blue Cross and Blue Shield; that relationship, however, to be consistent with the same existing relationship between the Maine Medical Association and all Health Insurance Carriers.

Dr. Robertson also stated that the Executive Committee is reviewing all Standing and Special Committees, usually taking up at least one committee each month to find out how valuable it is and whether or not it is functional. He also stated that the Legislative Committee has to spend many hours going over all the various bills affecting the Medical Community. The Secretaries and Presidents of the Medical Societies and Delegates are usually kept informed of the work of the Legislative Committee and of the

various bills being presented.

Dr. Brinton T. Darlington was a member of the Legislative Committee and he stated that they formerly shared a Counselor with Blue Cross and Maine Hospital Association and now, Blue Cross wanted to utilize the Counselor more, so the Maine Medical Association was forced to hire a new lawyer; one residing in Augusta was selected. This will be more expensive but will probably be more helpful.

Dr. Robertson stated that the increased cost of Medical dues was due to many things, such as change and location of the Headquarters, plus inflation and many other costs. He presented copies of a budget which was available for perusal.

The next meeting will be held the last of March at Down East Community Hospital, Machias, Maine.

KARL V. LARSON, M.D., *Secretary*

Piscataquis

The Piscataquis County Medical Society held its February meeting on the 27th at TJ's Restaurant in Dexter. Attendance was remarkable in that all but one active member was present and he was in Florida. Present, also, were spouses and three guests.

The program was presented by Dr. George Wood, noted Phthisiologist from Bangor. His subject was "Tuberculin Testing in Hospital Personnel." There was considerable discussion on the present management of the Tuberculin positive patient. The topic was well received.

Dr. Felix M. Garcia-Rey introduced the problem of the Milo practice situation and a committee was formed to outline means of cooperation between the Milo Community Hospital and Mayo Regional Hospital at the staff level.

Dr. Paul A. Fichtner of Greenville outlined the plight of the small rural hospital very well and discussion followed.

Dr. Charles H. Lightbody reported for the Executive Committee of the M.M.A., as did Dr. Joseph B. Alley for the Health Finance Committee.

Officers for the year starting in June were elected:

President: Dr. Lloyd M. Van Lunen, Jr., Dover-Foxcroft

Secretary-Treasurer: Dr. Charles H. Lightbody, Guilford

Member of the Executive Committee, M.M.A.: Dr. David P. Frasz, Dover-Foxcroft

Member of the House of Delegates, M.M.A.: Dr. Leslie M. Fernow, Dover-Foxcroft

Alternate, House of Delegates, M.M.A.: Dr. James W. Berry, Dover-Foxcroft

Representative to Health Finance Committee: Dr. Joseph B. Alley, Dover-Foxcroft

Dr. Charles H. Stone, III discussed the irony of a State and Federal regulation which requires all potential Hysterectomy patients, whether fertile or not, to sign a sterilization permit before surgery. He requested the M.M.A. introduce legislation correcting this inconsistency.

The following resolution was adopted to be presented to the House of Delegates of the M.M.A.:

WHEREAS—Mutual cooperation between the M.M.A. and the M.O.A. has become more and more a fact of life, and

WHEREAS—this cooperation is seen as an advantage to the welfare of the Citizens of Maine, and

WHEREAS—the Maine Osteopathic Association now recognizes dual membership in Medical Societies

RESOLVED: That if an Osteopathic Physician is a member in good standing in the M.O.A. and the A.O.A., he be allowed to be a member of the County Medical Society of the M.M.A. in the county in which he lives; with all the rights and privileges and responsibilities therein; providing he pays the appropriate dues to that County Medical Society.

Ed. Note: In accordance with a resolution approved by the M.M.A. House of Delegates on June 6, 1976, membership in the Maine Medical Association is contingent upon and compulsory with membership in a component county medical society.

The meeting was adjourned at 11:00 p.m. The next meeting to be held at the Lightbody Camp on Whetstone Pond on May 21, 1980.

CHARLES H. LIGHTBODY, M.D., *Secretary*

News, Notes and Announcements

Sixth Annual Maine Biomedical Science Symposium

The Sixth Annual Maine Biomedical Science Symposium will be held June 12-13, 1980 at the University of Maine at Orono. A forum is provided to report on clinical and basic research projects, either completed or in progress, to explain new methods or techniques, to hear of new developments in selected fields, and for open discussion among participants. The meeting is open to all interested participants. The major plenary session will be on Environmental Health, while concurrent sessions will be held on:

Behavior: Clinical Research	Genetics
Biological Membranes	Immunobiology
Cell and Molecular Biology	Nutrition
Clinical Medicine	Physiology and Aging
Environmental Health	Reproduction and Developmental Biology

The sixth symposium will feature several invited distinguished speakers, commercial and scientific exhibits, and a social hour and banquet for participants.

To submit a paper, or for other information, please contact either Dr. Muriel T. Davisson, The Jackson Laboratory, Bar Harbor, Maine 04609, Tel. (207) 288-3371 or Dr. Donald B. Mountcastle, Bennett Hall, University of Maine at Orono 04469, Tel. (207) 581-7826, 7546.

Seminar on Sports Medicine

A continuing medical education seminar will be presented by Regional Memorial Hospital and Bowdoin College on June 30- July 3, 1980, meeting criteria for twenty credit hours in Category I of Physician's Recognition Awards of the A.M.A. This seminar is designed for physicians and others involved with scholastic and collegiate athletics and/or adults in recreational and exercise programs.

For further information contact: Office of Continuing Medical Education, Regional Memorial Hospital, 58 Baribeu Dr., Brunswick, Maine 04011, telephone 207-729-0181, ext. 260.

Seminar On Current Topics In Pediatrics

Fourth annual seminar, Current Topics in Pediatrics, July 15-18, 1980. Colby College, Waterville, Maine. Sixteen hours Category I, P.R.A. Course Director: Leo Stern, M.D., Chairman of Pediatrics, Brown University. Faculty includes: Drs. John Kirkpatrick, Ronald Lauer, Conrad Wesselhoeft, Donald Klein, James Herndon, Arnold Gold, Lawrence Gartner and Mary Arnold. Emphasis on pediatric radiology, cardiology, surgery, orthopedics, allergy, neurology, neonatology and endocrinology. Families welcome. Inquiries and printed program: Robert H. Kany, Special Programs, Colby College, Waterville, Maine 04901.

Maine Association for Human Genetics Scholarship Program

1. Name:

Maine Association for Human Genetics Annual Scholarship.

2. General Description:

The MAHG Student Prize is a scholarship award based on a competitive review of original papers submitted by students attending a Maine college or University. Topics of papers will be limited to the general area of mammalian genetics including human genetics. Papers will report the results of studies performed by the student. Papers will be reviewed and judged by a committee of the MAHG. Decision of the judges will be final.

The award will be presented to the institution designated by the winning student for the specific purpose of defraying a part of that student's tuition. The award for the 1980 program will be \$500.00.

The winning paper and a number of selected papers among those submitted will be presented by the authors at the genetic session of the Annual Maine Biomedical Science Symposium to be held at the University of Maine in Orono early in June.

3. Eligibility Requirements:

Any student currently enrolled in an undergraduate program in any Maine college or University is eligible to submit a paper. Since it is anticipated that the prize will be used for tuition during the fall semester of 1980, students who are currently seniors should be matriculating into a graduate or professional school. The intent of the prize is to promote continued education in the area of genetics. Therefore, the award can be used solely for tuition purposes. Any student deciding not to pursue his or her education will be deemed ineligible. The prize may also be used for tuition due for previous semesters.

4. Format of Papers:

Papers will follow traditional format of scientific publications and will include the following sections: Introduction, Materials, and Methods, Results, Discussion and List of References. Papers will be limited to ten typewritten pages, double-spaced. Three copies of the paper will be submitted. Photocopies are acceptable but photographs should be submitted in triplicate.

5. Submission of Papers:

Deadline for submission will be April 15, 1980. Papers should be mailed to Dr. Laurent J. Beauregard, Genetic Program, Eastern Maine Medical Center, Bangor, Maine 04401.

6. Announcement of Award

Announcement of award will be made by May 15, 1980. Presentation will be made during the Fifth Annual Maine Biomedical Symposium to be held at the University of Maine at Orono on June 12 through 15.

Winning student is expected to present his or her paper at the genetic session of the symposium.

State of Maine Department of Human Services Division of Child Health Clinic Schedule—1980

By Appointment Only

Orthopedic Clinics

Bangor—St. Joseph Hospital

9:00 a.m.: Mar. 27, Apr. 24, May 22, June 26, July 24, Aug. 28, Sept. 25, Oct. 23, Nov. 20, Dec. 18

Fort Kent—Northern Maine Medical Center

9:00 a.m.: Mar. 11, May 13, July 15, Sept. 9, Nov. 4

Houlton—Houlton Regional Hospital

10:00 a.m.: Mar. 10, May 12, July 14, Sept. 8, Nov. 3

Presque Isle—A.R. Gould Memorial Hospital

9:00 a.m.: Mar. 12, May 14, July 16, Sept. 10, Nov. 5

Waterville—Mid-Maine Medical Center (Seton Unit)

Time scheduled by hospital: Mar. 3, Apr. 7, May 5, June 2, Sept. 8, Oct. 6, Nov. 3, Dec. 1

Cleft Palate Clinic

Portland—Maine Medical Center

9:00 a.m.: Mar. 17, May 19, June 16, Sept. 15, Oct. 20, Nov. 17

Cardiac Clinics

Bangor—St. Joseph Hospital

9:00 a.m.: Mar. 14, Apr. 11, May 9, June 13, July 11, Aug. 8, Sept. 12, Oct. 10, Nov. 14, Dec. 12

Portland—Maine Medical Center

9:00 a.m.: Mar. 7, 14, 21, 28, Apr. 4, 11, 18, 25, May 2, 9, 16, 23, June 6, 13, 20, 27, July 11, 18, 25, Aug. 1, 8, 15, 22, Sept. 5, 12, 19, 26, Oct. 3, 10, 17, 24, Nov. 7, 14, 21, Dec. 5, 12, 19

Children's Development Clinic

Lewiston—Central Maine Medical Center

8:30 a.m.: Mar. 10, Apr. 14, May 12, June 9, July 14, Aug. 11, Sept. 8, Nov. 10, Dec. 8

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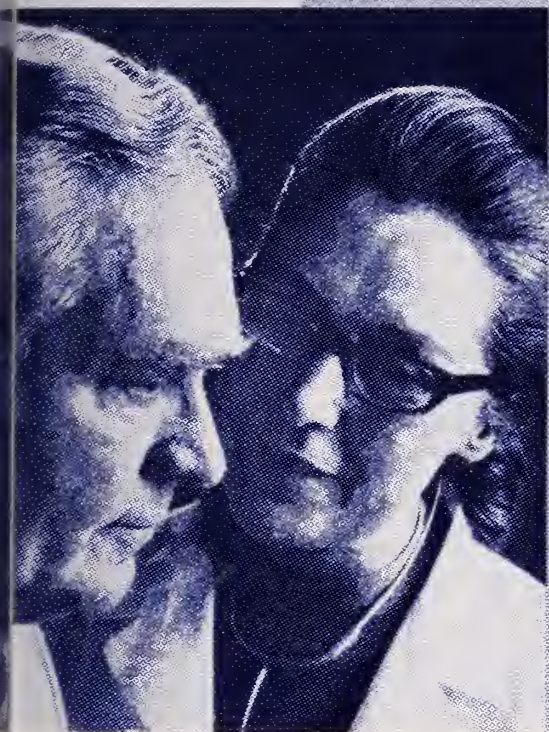


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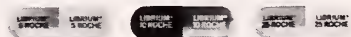
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Contraindications: Patients with known hypersensitivity to the drug

Warnings: Warn patients that mental and/or physical abilities required for tasks such as driving or operating machinery may be impaired, as may be mental alertness in children, and that concomitant use with alcohol or CNS depressants may have an additive effect. Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression, suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants, causal relationship has not been established clinically.

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County Society Notes

Androscoggin

The meeting of the Androscoggin County Medical Association was called to order by the President, Dr. Lawrence A. Nadeau, at 7:30 p.m. at Chase Hall, Bates College in Lewiston on December 20, 1979.

The first item of business was a vote accepting the printed minutes of the November 15, 1979 meeting as presented.

Dr. Nadeau then introduced Mr. Frank Stred, Executive Director of the M.M.A., a guest for the evening. Fifty-three members were present along with three guests, Mr. F. Stred—M.M.A., Mr. George Geyerhan—Media Specialist at CMMC and Juliette Giguere, R.N.

Correspondence was then read. This included: (1) YMCA letter of thanks, (2) Letter from PTO-PSR, and (3) Letter from M.M.A.

Following these items came the presentation of a new application for membership. This was the application of Dr. Gerald Phaneuf. A motion was made, seconded and passed that Dr. Phaneuf's application be accepted.

Dr. Frederick C. Holler then gave a brief report on the House of Delegates meeting which took place on November 17, 1979.

Following this came the presentation by the nominating committee, chaired by Dr. Louis N. Fishman, of the nominated slate of officers and councilors for 1980. These were:

President: Dr. Leo E. Cousineau, Lewiston

Vice President: Dr. Andre P. Marcotte, Lewiston

Secretary-Treasurer: Dr. Edward Z. Walworth, Lewiston

State Councilor: Dr. Gilbert R. Grimes, Lewiston (with term to expire in 1983)

County Councilor: Dr. James V.I. O'Sullivan, Lewiston (with term to expire in 1982)

A motion was made by Dr. Fishman and seconded by Dr. Gerard L. Morin that this slate be elected as proposed. All were in favor and the secretary cast one ballot. Dr. Nadeau then gave a brief address as the out-going president and expressed his thanks and appreciation.

A tribute to Juliette Giguere, R.N. followed. She was presented with a corsage and a check for her 28 years as Assistant Secretary to the ACMA.

The evening was concluded with an entertaining slide presentation by the irreplaceable Ivor O'Sullivan, M.D.

The meeting adjourned at 8:45 p.m.

The meeting of the Androscoggin County Medical Association was called to order at 7:30 p.m. by the President, Dr. Leo Cousineau. The meeting was held at Chase Hall, Bates College in Lewiston on January 17, 1980.

Forty-seven members were present and guests included Dr. David Phillips, Dr. Peter Leadley and Bruce Mason, D.D.S.

Printed minutes of the previous Association meeting were distributed and a motion was made that these be accepted. All were in favor.

Dr. Walworth briefly reviewed the minutes of the past Executive Committee meeting.

Following this Dr. Cousineau reviewed the list of Standing Committees. It was decided to retain the same Finance Committee as in 1979 and a new slate of Delegates and Alternates was voted into office. All other committees will be formed as the need arises.

Dr. Michael J. Harkins, chairman of the Finance Committee, then gave a report of the year-end financial investments.

Dr. Gilbert R. Grimes gave a brief report on the previous meeting of the Maine Medical Association Executive Committee.

Dr. Frederick C. Holler then made a motion regarding PSRO which was distributed to the members. Dr. Holler read the motion and explained his reasons for it point by point.

Dr. Phillips then gave an outline of the history, development and finances of PTO-PSR and, along with Dr. Leadley, answered questions from the members.

Following this, Dr. Holler's motion was brought to a vote. It was passed virtually unanimously with two abstentions.

The meeting adjourned at 8:50 p.m.

The Annual Meeting of the Corporators of the Androscoggin
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Officers of the Maine Medical Association—1979-1980

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CRAIG W. YOUNG, M.D., Presque Isle	Aroostook	1981
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HARRY A. BLISS, M.D., Portland	Ex-Officio	1980

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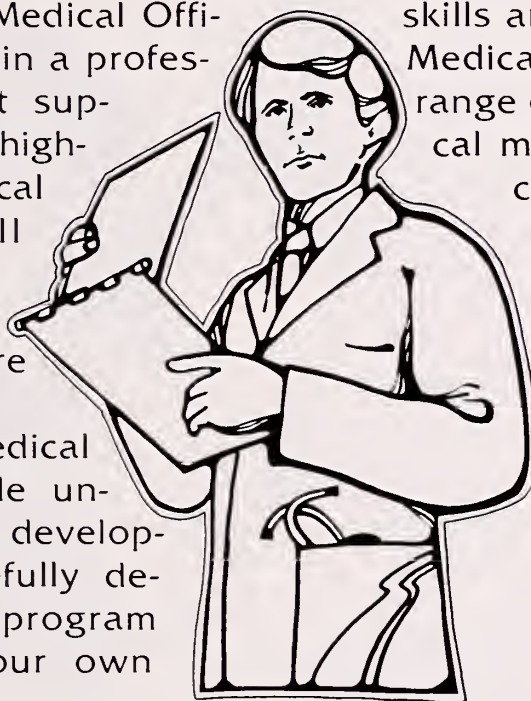
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The Journal of the Maine Medical Association

Volume Seventy-one

Augusta, Maine, May 1980

Number 5

Program — 127th Annual Session Maine Medical Association

June 12, 13, 14, 15, 1980

Arranged by the Scientific Committee

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Dr. Whitten

The Scientific Program of the annual meeting of the Maine Medical Association is made possible by the cooperation and assistance of the Technical Exhibitors and the following organizations:

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Medicine

Maine Chapter, American College of Physicians

Maine Psychiatric Association

For this cooperation and support, the members of the Scientific Committee are grateful.

Information

Registration:

Registration throughout the session will be in the Main Lobby at The Balsams.

Thursday, June 12—9:00 A.M. to 5:00 P.M.

Friday, June 13—8:00 A.M. to 5:00 P.M.

Saturday, June 14—8:00 A.M. to 5:00 P.M.

Sunday, June 15—8:00 A.M. to 3:00 P.M.

Telephone: The number at The Balsams in Dixville Notch, NH (603) 255-3400.

Meal Tickets:

For those not registering in the hotel, meal tickets may be purchased at the hotel reservation desk.

Visiting Delegates:

Introduction of Visiting Delegates will take place at meetings of the House of Delegates on Thursday, June 12 and Friday, June 13.

Technical Exhibits:

This year, seventeen companies are contributing to the success of the annual session program by participating in

the Technical Exhibits. A list of the exhibiting companies and representatives will be found on pages 134 and 135 of this program.

Please show your appreciation for the support of these companies by visiting these exhibits.

Badge Code:

Badges with green borders indicate Past Presidents, Delegates and Alternate Delegates of the M.M.A.; yellow borders, Executive Committee and members of the M.M.A.; blue borders, guests; and red borders, exhibitors.

Thursday, June 12

8:00 to 9:30 A.M. BREAKFAST—Main Dining Room

10:00 A.M. Executive Committee Meeting

12:30 to 2:00 P.M. LUNCHEON—Main Dining Room

2:00 P.M. First Meeting of the House of Delegates

Call to Order: BRINTON T. DARLINGTON, M.D., President

Presiding: GEORGE W. BOSTWICK, M.D., Speaker of the House

Presentation of the A.H. Robins' Physician Award for Community Service

5:00 P.M. Reference Committee Members' Meeting

6:00 P.M. COCKTAILS (Cash Bar) — John Dix Social Room

7:00 P.M. DINNER—Main Dining Room
Movie in the Theater

9:30 P.M. MUSIC AND DANCING in the Wilderness Room

Friday, June 13

8:00 to 9:30 A.M. BREAKFAST—Main Dining Room

8:30 A.M. Reference Committee Meetings

12:30 to 2:00 P.M. LUNCHEON—Main Dining Room

2:00 P.M. Second Meeting of the House of Delegates

Election of President-elect and Executive Committee Members

Executive Committee Meeting Immediately Following House of Delegates

6:00 P.M. COCKTAIL PARTY—John Dix Social Room

7:00 P.M. DINNER—Main Dining Room

9:30 P.M. MUSIC AND DANCING—Ballroom
Entertainment

9:30 P.M. MUSIC AND DANCING in the Wilderness Room

Saturday, June 14

8:00 to 9:30 A.M. BREAKFAST—Main Dining Room

8:00 A.M. Executive Committee Breakfast Meeting

Scientific Program

8:30 A.M. to 1:00 P.M.

Welcome—DANA M. WHITTEN, M.D.

8:30 A.M. "Controlling" Diabetes — Does it Really Matter?

WILLIAM C. ERVIN, M.D., Portland

9:30 A.M. HEMATOLOGIC MALIGNANCY SESSION

Lymphoma — Which, When and How to Treat

JANE T. DESFORGES, M.D., Boston

Childhood Leukemia: Changing Prognosis

CAROL A.C. CROWLEY, M.D., Boston

10:45 A.M. COFFEE BREAK

11:00 A.M. THYROID NODULES SESSION

Selecting the Patient for Thyroid Biopsy and Surgery

RICHARD C. EASTMAN, M.D., Portland

Surgical Approach to Thyroid Nodules

WALTER B. GOLDFARB, M.D., Portland

11:30 A.M. The Scabies Scourge

THOMAS L. WATT, M.D., Bangor

11:45 A.M. SESSION ON THE BACK

Chiropractic

ROBERT E. MCAFEE, M.D., Portland

Scoliosis — A Review of Current Treatment

ROBERT B. KELLER, M.D., Belfast

12:30 to 2:00 P.M. LUNCHEON—Main Dining Room

6:00 P.M. COCKTAIL PARTY—John Dix Social Room

7:00 P.M. Annual Banquet—Main Dining Room

Presentation of Honorary Pins

President's Address: BRINTON T. DARLINGTON, M.D.

Presentation of President's Award for Distinguished Service

9:30 A.M. MUSIC AND DANCING—Ballroom
Entertainment

9:30 P.M. MUSIC AND DANCING in the Wilderness Room

Sunday, June 15

8:00 to 9:30 A.M. BREAKFAST—Main Dining Room

8:00 A.M. Executive Committee Breakfast Meeting

Scientific Program

8:30 A.M. to 1:00 P.M.

Welcome—DANIEL H. WOOD, M.D.

8:30 A.M. PANEL ON TRAUMA

RICHARD C. BRITTON, M.D., Portland, and assistants

9:30 A.M. ENDOCRINOLOGY/GYNECOLOGY SESSION

Estrogens

BRUCE F. BOWER, M.D., Hartford

Dysmenorrhea — An Enigma

MARGARET E. DENSMORE, M.D., Belfast and Bangor

10:30 A.M. COFFEE BREAK

10:45 A.M. Developments in the Neurosurgical Treatment of Cerebellopontine Angle Tumors

EDWARD C. TARLOV, M.D., Boston

11:30 A.M. Topical Talk on Tropical Travel: Preparing the Patient Who Wants to Leave Maine and What to Look for When He/She Gets Back

LEONARD C. MARCUS, V.M.D., M.D., Boston

12:15 P.M. Soviet Sports Medicine

DANIEL F. HANLEY, M.D., Brunswick

12:30 to 2:00 P.M. LUNCHEON—Main Dining Room

Specialty Group Meetings

Saturday, June 14

12:30 P.M.—Main Dining Room

Luncheon Meeting

OFFICERS AND COUNCIL OF THE MAINE CHAPTER, AMERICAN COLLEGE OF PHYSICIANS

HARRY A. BLISS, M.D., Portland, presiding

VISIT

THE TECHNICAL

EXHIBITS

BEFORE AND AFTER EACH
SESSION AND DURING INTERMISSIONS

2:00 P.M. MAINE SOCIETY OF ALLERGY AND CLINICAL IMMUNOLOGY

ROBERT J. BARRETT, JR., M.D., Bangor, President, presiding

Annual Business Meeting

Speaker: To be announced

Subject: **Current Status of Stinging Insect Venom Therapy**

2:00 P.M. MAINE SOCIETY OF EYE PHYSICIANS AND SURGEONS

ANDREW J. GAY, M.D., Belfast, President, presiding

Business Meeting

2:00 P.M. MAINE CHAPTER, AMERICAN COLLEGE OF PHYSICIANS

HARRY A. BLISS, M.D., Portland, presiding

Business Meeting

3:00 P.M. MAINE CHAPTER, AMERICAN SOCIETY OF INTERNAL MEDICINE

LEOPOLD A. VIGER, M.D., Biddeford, President and
GEORGE E. DAVIS, JR., M.D., Augusta, President-elect, presiding

Business Meeting

Speaker: JOHN F. FARRINGTON, M.D., President, American Society of Internal Medicine

Sunday, June 15

12:30 P.M.—Main Dining Room

Luncheon Meeting

MAINE SOCIETY OF GASTROENTEROLOGY

GEORGE E. DAVIS, JR., M.D., Augusta, President, presiding

12:30 P.M.—Main Dining Room

Luncheon Meeting

MAINE PSYCHIATRIC ASSOCIATION

RICHARD EVANS, III, M.D., Brunswick, President-elect, presiding

2:00 P.M. MAINE CHAPTER, AMERICAN ACADEMY OF FAMILY PHYSICIANS

HAROLD N. BURNHAM, M.D., Gorham, President, presiding

Business Meeting

3:00 P.M. MAINE PSYCHIATRIC ASSOCIATION

RICHARD EVANS, III, M.D., Brunswick, President-elect, presiding

Business Meeting

Speaker: PETER E. SIFNEOS, M.D., Beth Israel Hospital, Boston

Subject: **Short-term Psychotherapy**

HONORARY PINS

Presentation of the Association's Honorary Pins will be made by Brinton T. Darlington, M.D., President of the M.M.A. at the Annual Banquet, Saturday evening, June 14 at 7:00 P.M.

FIFTY-YEAR LAPEL PINS

Fifty-Year Lapel Pins will be presented to the following members who were graduated from Medical School in 1930:

Cumberland County

Roderick L. Huntress, M.D.
Boston University School of Medicine

Thor Miller, M.D.
Boston University School of Medicine

Alvin A. Morrison, M.D.
Harvard Medical School

Kennebec County

Harvey J. Bourassa, M.D.
Boston University School of Medicine

Clarence R. McLaughlin, M.D.
Boston University School of Medicine

Lincoln-Sagadahoc County

Fuller G. Sherman, M.D.
Jefferson Medical College

FIFTY-FIVE-YEAR LAPEL PINS

Fifty-Five-Year Lapel Pins will be presented to the following members who were graduated from Medical School in 1925:

Cumberland County

John J. Lappin, M.D.
New York University School of Medicine

Alice A.S. Whittier, M.D.
Yale University School of Medicine

SIXTY-YEAR LAPEL PINS

Sixty-Year Lapel Pins will be presented to the following members who were graduated from Medical School in 1920:

Cumberland County

Winifred W. Curtis, M.D.
Boston University School of Medicine

Isaac M. Webber, M.D.
Bowdoin Medical School

Kennebec County

Blynn O. Goodrich, M.D.
McGill University Faculty of Medicine

Knox County

George Loewenstein, M.D.
Friedrich Wilhelms University

Oxford County

James A. Mac Dougall, M.D.
McGill University Faculty of Medicine

SIXTY-FIVE-YEAR LAPEL PIN

A Sixty-Five-Year Lapel Pin will be presented to the following member who was graduated from Medical School in 1915:

Cumberland County

Elton R. Blaisdell, M.D.
Bowdoin Medical School

“Medicine Avenue”

Technical Exhibits

Armour Pharmaceutical Company, P.O. Box 1849,
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Encyclopaedia Britannica—USA, 425 North Michigan
Ave., Chicago, Illinois 60611
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Wolf Randon

Lederle Laboratories, Pearl River, New York 10965

Eli Lilly and Company, 307 E. McCarty St., Indianapolis,
Indiana 46285

Maine Medical Practice Management Association, 54
Arsenal St., Augusta, Maine 04330

Maine National Bank, 400 Congress St., Portland, Maine
04101

Representatives: Ms. Barbara J. Weldon and Ms.
Gail C. Foust

McNeil Laboratories, Inc., 500 Office Center Dr., Fort
Washington, Pennsylvania 19034
Representatives: Mr. Joe Ruest and Mr. Ron Clark

Mead Johnson Nutritional Division, 2404 Pennsylvania
Ave., Evansville, Indiana 47721
Representatives: Ms. Diane Meekins, R.D., Mr. Guy
F. Hunter, Jr. and Mr. Remi St. Onge

Organon Pharmaceuticals, 375 Mt. Pleasant Ave., West
Orange, New Jersey 07052
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Richard Wroe

Ortho Pharmaceutical Corporation, Raritan, New Jersey
08869
Representatives: Mr. Marshall Stewart and Mr.
Ronald M. Bernarducci

Pfizer Laboratories, 230 Brighton Rd., Clifton, New Jersey 07012

Representatives: Mr. Joe Balassone, Mr. Billy Graham and Mr. C. Jankoski

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Representative: Mr. Wayne Jackson

Searle Laboratories, Box 5110, Chicago, Illinois 60680

Representatives: Mr. Al Grimes and Mr. Tom Ordway

U.S. Army Medical Department, U.S. Army Surgeon General's Office, 1900 Half St., S.W., Washington, D.C. 20324

Representative: Captain Richard H. Griswold

Visiting Delegates

The Connecticut State Medical Society
BENJAMIN M. SHENKER, M.D., Middletown

New Hampshire Medical Society
WILLIAM H. GIFFORD, M.D., Colebrook

The Rhode Island Medical Society
ROBERT L. CONRAD, M.D., Wakefield

Vermont State Medical Society
JOHN LEPPMANN, M.D., Bellows Falls

COUNTY SOCIETY NOTES—Continued from Page 126

County Medical Association, Inc. was called to order at 7:40 p.m. by the President, Dr. Leo E. Cousineau.

The meeting was held on February 21, 1980 at Chase Hall, Bates College in Lewiston with 44 members present. Guests included Drs. Patrick A. Dowling and Jeremy R. Morton of Cumberland County and James Vaccarino, Esq.

Printed minutes of the meeting held January 17, 1980 were distributed and accepted.

Dr. Walworth reviewed the previous meeting of the Executive Committee, and went on to review the results of the State Nomination Committee meeting. Nominated as President-elect for 1980-1981 were Drs. David L. Phillips and George W. Bostwick.

Those nominated to M.M.A. Committees from this county (A) and those currently serving terms (B) are:

- (A) Dr. Gilbert R. Grimes: Executive Committee (3 yrs.)
- (B) Dr. Michael C. Bach: Comm. on Continuing Education (1 yr.)
- (B) Dr. David D. Smith: Comm. on Recruitment, Aid & Placement (2 yrs.)
- (A) Dr. Margaret H. Hannigan: Comm. on Recruitment, Aid & Placement (3 yrs.)
- (B) Dr. David D. Smith: Comm. on Scientific Programs (1 yr.)
- (A) Dr. Barry D. Chandler: Comm. on Scientific Programs (3 yrs.)
- (A) Dr. Larry O. Hopperstead: Comm. on Emergency Medical Services (3 yrs.)
- (A) Dr. Edward Z. Walworth: Comm. on Emergency Medical Services (3 yrs.)
- (B) Dr. Leo E. Cousineau: Comm. on Government Health Activities (2 yrs.)
- (A) Dr. Frederick C. Holler: Comm. on Government Health Activities (3 yrs.)
- (B) Dr. Frederick C. Holler: Comm. on Health Care Financing (1 yr.)
- (B) Dr. Thomas F. Shields: Comm. on Ethics, Discipline & Prof. Comp. (2 yrs.)
- (B) Dr. Leo E. Cousineau: Comm. on Legislation (2 yrs.)

Following these announcements, printed copies of the 1979 Financial Statement were circulated and voted on. This was accepted unanimously.

The featured speaker for the evening was Mr. James Vaccarino of Johnson & Higgins, Consultants to Medical Mutual Ins. Co. of Maine. Mr. Vaccarino addressed the members on the subject of loss prevention in a medical setting.

The meeting adjourned at 9:07 p.m.

EDWARD Z. WALWORTH, M.D., *Secretary*

Oxford

The January meeting of the Oxford County Medical Society was held on Wednesday, January 9, 1980 at the Bethel Inn in Bethel.

This meeting was attended by thirteen active members of the Society.

Dr. Linwood M. Rowe, President of the Oxford County Medical Society, called the meeting to order.

We were pleased to have the opportunity to meet the Executive Director of the Maine Medical Association, Mr. Frank O. Stred, who discussed briefly the financial aspects of the newly acquired building by the Maine Medical Association in Augusta. He also brought us up to date on recently passed legislation as well as legislation pending before the House of Delegates. Mr. Stred expressed deep appreciation for the excellent work done by Dr. Dan Hanley for our Association.

The next meeting is scheduled for Wednesday, March 12, 1980 at Madison's Restaurant in Rumford.

There being no new business, the meeting was adjourned.

USHA WADHERA, M.D., *Secretary*

Kennebec

The Kennebec County Medical Association met at Guido's Wine Cellar in Augusta on March 21, 1980 with 31 members and one guest in attendance. In the absence of Dr. John W. Towne, the President, Dr. Robert A. Stram called the meeting to order.

The application of Dr. John Engle for membership was read. The application of Dr. Robert Wise was voted on and Dr. Wise was welcomed into the membership of the Association.

The amendments to the Constitution and Bylaws which had been read at the January meeting were unanimously approved. These bylaw changes add the Maine Medical Association's Executive Committee member and a representative of each hospital staff in the County to the Council of the Association.

Following completion of the business session, Dr. Albert J. Pepe introduced Dr. Bob Johnson from the University of Vermont who gave a most interesting lecture on the biomechanics of skiing injuries based on various experiences which have been quite extensive.

The meeting was adjourned at 9:30 p.m.

O. THOMAS FEAGIN, M.D., *Secretary*

Combination Chemotherapy of Hairy Cell Leukemia With Cyclophosphamide, Vincristine and Prednisone

DELVYN C. CASE, JR., M.D., F.A.C.P.*

ABSTRACT

Chemotherapy for patients progressing after splenectomy for hairy cell leukemia has produced little benefit in earlier series. More recent work has documented responses to several agents given singly or in combination. The patient in this report achieved a partial remission with the combination of cyclophosphamide and vincristine, administered intravenously, and oral prednisone. During the period of 10 months while in remission, transfusions were not required and significant infections did not develop. Although progressive disease did eventually develop, combination chemotherapy with these agents and others shown to be active should be further studied.

INTRODUCTION

The chemotherapy of hairy cell leukemia has in the past produced disappointing results. Splenectomy as initial therapy produces sustained remissions in only one-third of cases;¹ and further treatment is required when progressive hematologic deterioration occurs. While some improvement has been noted with corticosteroids² and chemotherapy,^{1,3-9} serious and often fatal infectious complications have occurred as a result of immunosuppression and myelosuppression^{7,10,11} without remission. Recently encouraging results have been documented in patients treated with rubidazole¹² and low dose chlorambucil¹³ as single agents. Aggressive combination chemotherapy has produced remissions in a small number of reported cases.^{1,3-5,14} The following patient responded to combination chemotherapy consisting of cyclophosphamide, vincristine and prednisone, achieving a partial remission lasting 10 months.

CASE REPORT

A 51-year-old white female was admitted to the hospital for an 8-week history of fatigue, easy bruising, pallor and pancytopenia. Physical examination revealed multiple ecchymoses and an enlarged, firm spleen, 8 cm. below the left costal margin. There was no lymphadenopathy or hepatomegaly. Her hemoglobin (Hb) was 9.8 gm/dl, platelet count 12,000/ μ l, and WBC 1900/ μ l with 12% neutrophils, 11% band forms, 32% lymphocytes, and 35% hairy cells. Bone marrow aspiration revealed a "dry" tap; bone marrow biopsy revealed a cellular marrow with areas of fibrosis and infiltration by cells compatible with a diagnosis of hairy cell leukemia. Megakaryocytic, erythroid, and myeloid cell lines were markedly diminished. The tartrate-resistant acid phosphatase stain

was positive. Because of severe pancytopenia, splenectomy was performed. Postoperatively, there was a rapid rise in peripheral counts, achieving a Hb 10.0 gm/dl, platelet count 124,000/ μ l, and WBC 7900/ μ l, with 40% hairy cells by the time of discharge 2 weeks later.

Two months later the patient presented with progressive anemia, leukocytosis, and thrombocytopenia. Her Hb was 9 gm/dl, her platelet count was 60,000/ μ l, and her WBC was 11,900/ μ l with 99% hairy cells. Because of progressive disease, the patient was started on combination chemotherapy consisting of monthly cycles of cyclophosphamide, 600 mg/m² i.v. days 1 and 8, vincristine 1.4 mg/m² i.v. days 1 and 8, and prednisone 40 mg/m² p.o. days 1-14. After one cycle of therapy, the counts stabilized at Hb 12 gm/dl, platelet count 78,000/ μ l, and WBC 7300/ μ l with reduction in the proportion of hairy cells to 34%. After the second cycle of therapy, the platelet count rose to 100,000/ μ l. Between cycles of treatment, there was moderate myelosuppression; but full recovery occurred before each cycle. No significant infections or bleeding episodes occurred during therapy. For 10 months the patient remained symptom-free with stable counts and did not require transfusions. However, the patient continued to have 5-35% hairy cells in the periphery. Repeat bone marrow was not performed because of persistence of leukemia on peripheral smear.

After 11 months of therapy, progressive anemia, thrombocytopenia, and leukocytosis developed. The patient did not respond to two further cycles of cyclophosphamide, vincristine, and prednisone, nor to a combination of prednisone 20 mg/m²/day p.o., chlorambucil 6 mg/m²/day x 21 days of each cycle, and C.C.N.U. 100 mg/m² p.o. every 6 weeks. The patient expired from hemorrhage and sepsis 5 months after relapse.

DISCUSSION

Until recently the chemotherapy of hairy cell leukemia has produced little benefit and has been reported as harmful.^{7,10,14} Impaired marrow granulocyte reserve and leukocyte mobilization¹⁵ as well as abnormalities in the number and function of T lymphocytes^{2,8,14,16-20} and monocytes^{21,22} complicate the expected myelosuppression from chemotherapy. The low intrinsic mitotic rate of hairy cells in the marrow^{23,24} reduces the susceptibility to drugs. Intensive therapy with defective marrow reserve^{4,7} exacerbates the tendency toward infection. Earlier results have been disappointing with single agents, with only transient hematologic improvements seen in patients treated with vinca alkaloids, corticosteroids, and cytotoxic agents.^{3-6,8-11,25-30} Chlorambucil in low doses has been shown in a new series to produce long-term remissions in post-splenectomy patients with progressive leukemia.¹³ While Adriamycin[®] 27 has been previously used without success, two patients treated with rubidazole¹² have had remissions lasting 13 and 20 months.

The experience with combination chemotherapy has been limited. However, one patient has been reported who went into complete remission lasting 20 months with a combination of cyclophosphamide

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and cytosine arabinoside after failing vincristine and prednisone;⁴ while another patient treated with cytosine arabinoside, vincristine and prednisone had a partial remission.¹⁴ One case treated with vincristine and prednisone had a normal bone marrow biopsy 10 months later.⁵ A transient complete remission (5 months) had been reported with cyclophosphamide, vincristine and prednisone.³ Androgen and prednisone have also resulted in reversal of severe cytopenias.³¹

The patient presented in this report had a partial remission for 10 months with the combination of cyclophosphamide, vincristine, and prednisone. During this time, transfusions were not required. Because a significant reduction in the percentage of hairy cells in the periphery occurred (from 99% to 5-35%), along with a rise in the neutrophil count, significant infections did not develop. Expected myelosuppression did occur, but undue morbidity was avoided because of the significant yet only partial response. The bone marrow examination was not repeated because of the persistence of leukemia in the periphery. Unfortunately because only a partial remission was achieved, relapse developed after only 10 months. The patient then succumbed to drug- and disease-induced myelosuppression without remission induction.

The results in this paper as well as other recent studies suggest that hairy cell leukemia is responsive to a number of chemotherapeutic agents, and that significant remissions, even long-term remissions, can be achieved. A combination that might include rubidazone, cytosine arabinoside, and the agents used in this paper, cyclophosphamide, vincristine and prednisone, might be considered in patients too severely ill to undergo splenectomy, or in those patients post-splenectomy who demonstrate marked deterioration in hematologic parameters.

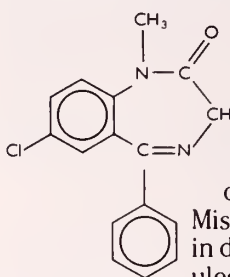
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It should be emphasized that there is no "magic" in any anti-anxiety tablet; that medication is not prescribed as a problem solver. Instead, Valium is being prescribed *as a temporary measure to relieve symptoms* generated by excessive anxiety and psychic tension.



* Boyd JR, et al: *Am J Hosp Pharm* 31: 485-491, May 1974

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety associated with anxiety disorders, transient situational disturbances and functional or organic disorders, psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms, or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal, adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy). The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

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possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication, abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic level at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider fully pharmacology of agents employed, drugs such as phenothiazines, narcotics

Practical pointers on taking antianxiety medications

do's Patients should be instructed to keep to their dosage schedule exactly as prescribed. If they miss a dose, they should not try to make it up by taking two doses the next time. Ask them to contact you promptly if they experience worrisome side effects.

Explain that drowsiness is a common reaction to almost all calming agents, but that it usually subsides in a few days. Urge the patient to contact you for a possible dosage adjustment if drowsiness or other reactions persist.

Just as you request a complete list of all medications the patient is taking, suggest that this list be given to any other physician treating her/him.

Like all medicines, Valium should be kept out of reach of children and young people. Old or unused medication should be discarded.

and don'ts Since drowsiness is an occasional problem, patients should be advised against driving or operating hazardous machinery until they see how the medication affects them. They should also know that tranquilizers increase the effects of alcoholic beverages, which should therefore be avoided. Also, warn patients against simultaneous use of drugs that depress the central nervous system, particularly sedative hypnotics.

Patients should be aware of the importance of not sharing their medications with friends and neighbors; they should know that what you have prescribed for them may be contraindicated for others.

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barbiturates, MAO inhibitors and other anti-depressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

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“Inside-Out and Bottom-Up”

A Philosophy of Facial Reconstruction Revisited

JEFFREY S. FISTER, D.M.D.* AND WILLIAM D. JONES, III, M.D.**

Modern modes of transportation have provided the surgeon with a steady supply of complex maxillofacial trauma. With the increase in the number of high speed motor vehicular accidents, there has been a corresponding increase in the number of multiple facial injuries. The isolated facial fracture or facial laceration generally presents little difficulty in the formation of a treatment plan which would restore the patient's original anatomy and function. However, those injuries consisting of multiple facial fractures or fractures coexisting with complex soft tissue wounds often result in less than satisfactory reconstruction if a systematic approach to the treatment sequence is not strictly followed. “Inside-out and bottom-up” is a phrase coined by E.W. Small in 1971, and it represents such a systematic approach in the treatment of all maxillofacial injuries.¹ The purpose of this paper is to indicate the need for a simplified approach to the treatment of all facial injuries, to describe the treatment sequence based on the premise “inside-out and bottom-up” and to point-out the pitfalls which result without strict adherence to this treatment sequence.

TREATMENT SEQUENCE

“Inside-out and bottom-up” is an organizational approach in the treatment of maxillofacial injuries; that is it dictates the treatment sequence to be followed in the treatment plan. “Inside-out” refers to the treatment of those wounds involving the oral cavity in a progressive manner from posterior to anterior. Prior to closure of facial lacerations, the intraoral injuries must be treated. The teeth should be replanted and repositioned, and the alveolar bone should be reduced and fixated following debridement. All intraoral lacerations needing closure should be sutured. Upper and lower arch bars or their equivalent should be placed at this time if more extensive facial fractures exist, even if more definitive treatment is not anticipated for several days. Only then should closure of facial lacerations be commenced. Through-and-through lip lacerations involving mucosal and skin surfaces must always be closed “inside-out,” that is, mucosal closure must be performed first, followed by closure of muscle and finally subcutaneous and cutaneous structures.

“Bottom-up” refers to the treatment of the facial bone fractures in a progressive manner from inferior to superior. In order to illustrate how the face is

rebuilt from “bottom-up,” schematic diagrams will be used (Figures 1-7). Figures 1 and 2 represent the facial bones in both facial and lateral views respectively. Figure 3 represents a patient with multiple facial injuries consisting of mandibular fractures, a LeFort II midfacial fracture, and bilateral zygomaticomaxillary complex fractures. After having treated all intraoral injuries, reconstruction of the face is begun by reestablishing the integrity of the mandible (Figure 4).

Once the mandibular teeth have been repositioned, the occlusion is the next complex presenting itself as the treatment progresses superiorly. Actually, the occlusion is the manner in which the upper and lower teeth interdigitate and it is the restoration of this occlusion that is the only key to relating the maxilla to the mandible (Figure 5).¹ In the figures the occlusion is represented by the white blocks which are “keyed” together (Figure 1 and 2). The position to which the patient would consistently (and predictably) return his teeth is referred to as the habitual occlusion, and it is important to recognize that there is one, and only

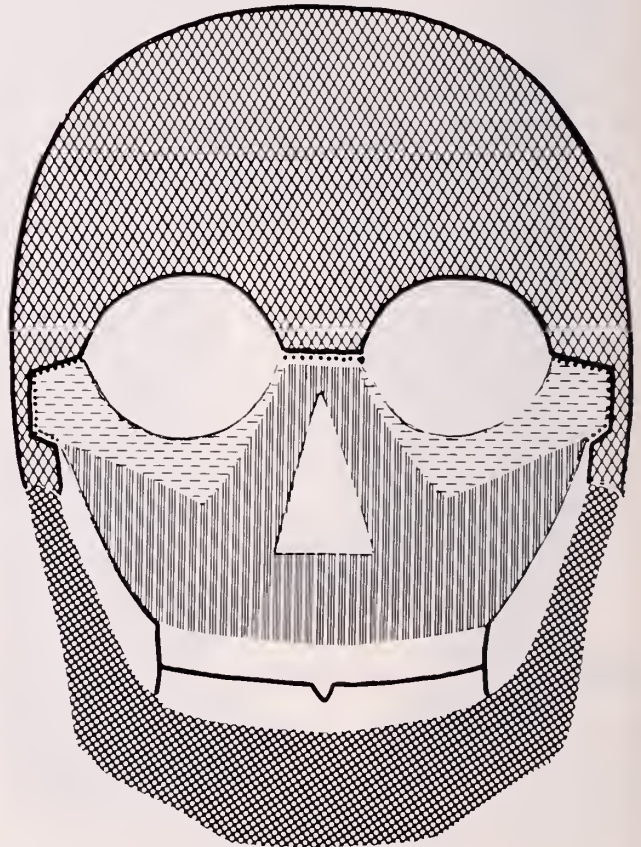


Fig. 1. Schematic diagram in frontal view of facial bones and cranium.

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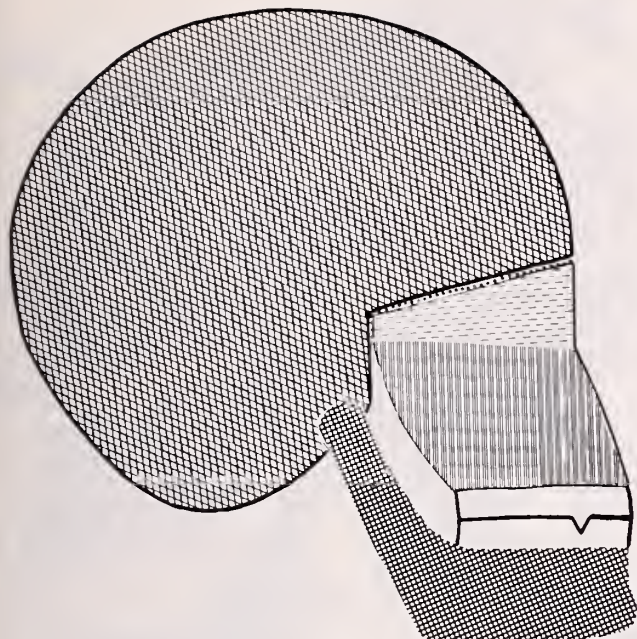


Fig. 2. Schematic diagram in lateral view of facial bones and cranium. Cranium is represented by fine cross-checking.

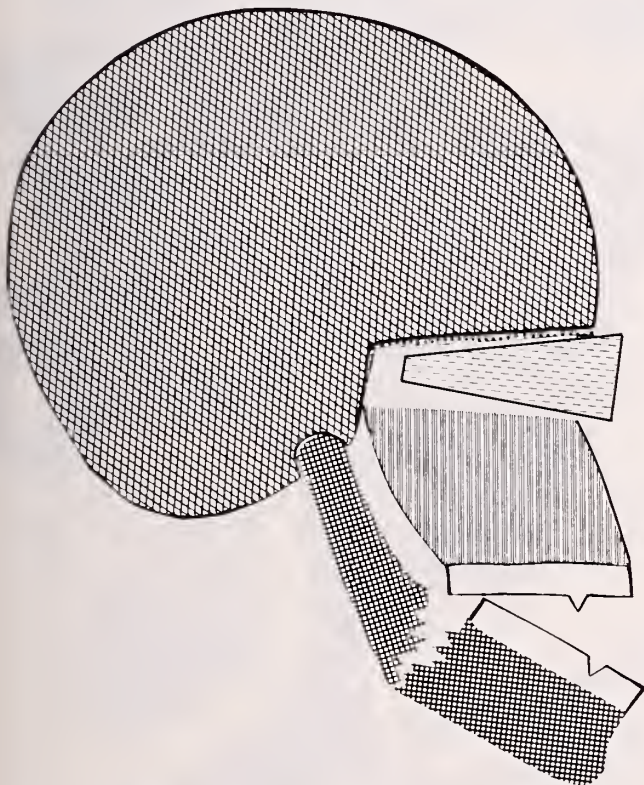


Fig. 3. Schematic representation of multiple facial fractures, including mandibular fracture(s), LeFort I midfacial fracture, and zygomaticomaxillary complex fracture(s).

one, habitual occlusion for every patient no matter what their tooth arrangement was prior to injury. Recognition of a patient's habitual occlusion depends on a thorough understanding of occlusal relationships, tooth position, and wear facets.

In the injury represented by Figure 3, the zygo-

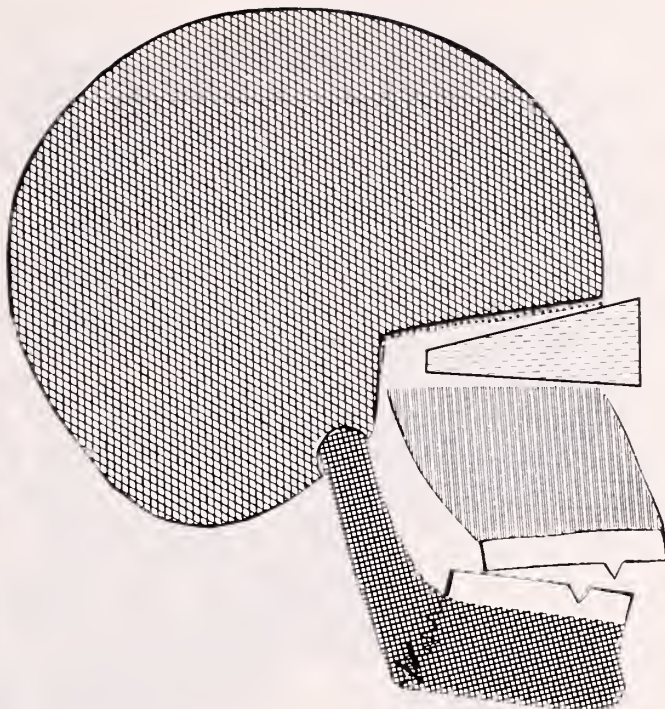


Fig. 4. Schematic representation of the first phase of facial reconstruction following the "Bottom-up" treatment sequence. Note the reduction of the mandible which establishes the anterior-posterior position of the rest of the facial bones.

maticomaxillary complexes (zygomax) are the most superior facial bones displaced, and therefore are the final structures to be reduced (Figure 6). Nasal bone fractures should be reduced and fixated following fixation of all other midfacial structures, and facial lacerations should be treated last.

DISCUSSION

It is important to recognize from the outset that maxillofacial injuries are commonly not life threatening, and therefore, once maintenance of the airway and control of hemorrhage has been accomplished, definitive management of facial injuries can often be deferred.^{1,2,3} Those patients requiring several days of observation prior to any operative procedure in an operating room setting would be best treated initially by temporarily immobilization of individual fractures by means of a closed technique (placement of arch bars, etc.) and, if possible, establishment of intermaxillary fixation. Closure of lacerations would also be indicated at this time, realizing that such a compromise is acceptable under these conditions.³ However, when the situation is such that other injuries must be cared for early in the operating room setting, then early concomitant treatment of facial injuries should also be considered.¹

When considering the overall spectrum of treatment for maxillofacial injuries, the basic principles in the treatment of fractures found in other parts of the body also pertain to the treatment of maxillofacial fractures (i.e., reduction, fixation, immobilization).⁴ The treatment sequence for each particular injury

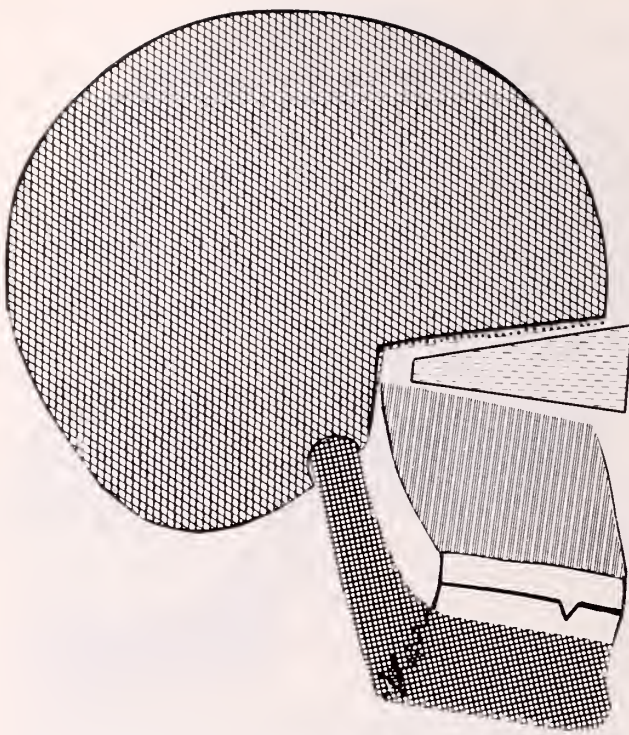


Fig. 5. Establishment of relative position of maxilla to the mandible through the existing occlusion. Note the exact interdigitation of the teeth.

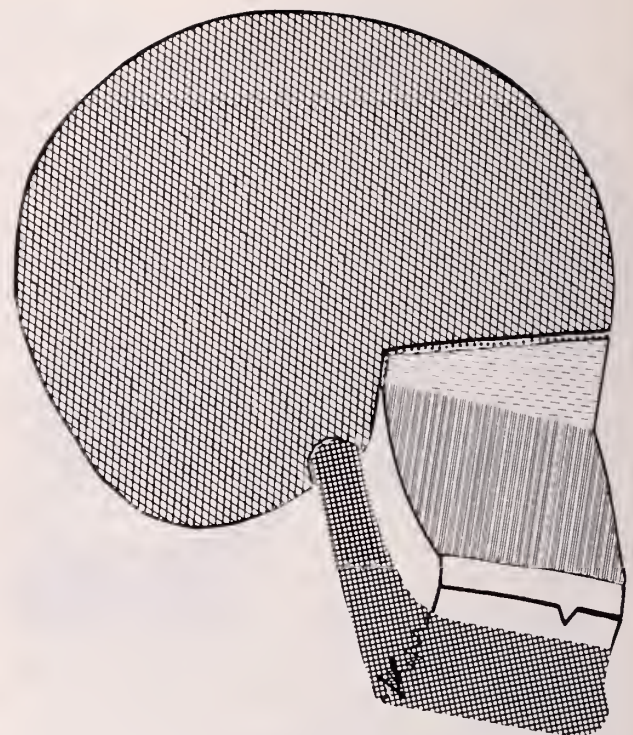


Fig. 6. Final phase in facial reconstruction showing the zygomas reduced.

(i.e., debridement, reduction, fixation, closure) is also the same. In addition to these, however, two basic guidelines *must* be followed for proper management of multiple maxillofacial injuries: proceed “inside-out and bottom-up” and reestablish habitual occlusion.¹

All intraoral injuries must be treated prior to closure of facial lacerations. If facial lacerations are treated prior to any intraoral procedures, excessive trauma will result to these closures as the intraoral injuries are treated, often resulting in wound contusion and sometimes suture tears. At the very least, closed facial wounds inhibit visualization and access to traumatized intraoral structures, and thus sometimes necessitate reopening these previously closed wounds in order to gain adequate access to the operative field. Likewise, as previously mentioned, through-and-through lip lacerations should be closed starting with mucosa and followed by closure of muscle and finally subcutaneous and cutaneous structures. Allowing the mucosa and submucosa to heal by secondary intent results in significant contracture with its obvious sequellae,³ while closing these structures initially seals saliva and oral contaminants from the wound, thus preventing possible wound infection and subsequent breakdown. Disregard for closure of circumoral musculature results in annular scar contracture with subsequent notching and surface depression.

As previously described, “bottom-up” refers to the treatment of the facial bone fractures in a progressive manner from inferior to superior. The sequence of treating from below and working up is

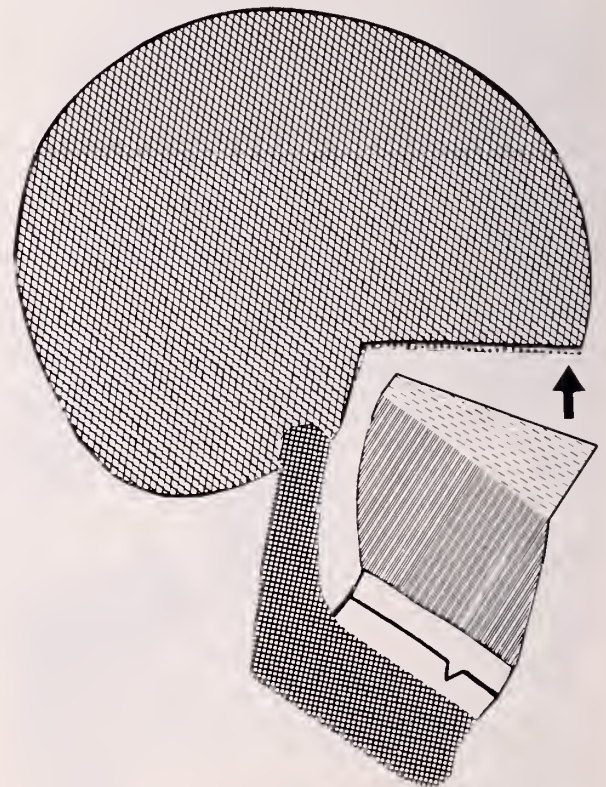


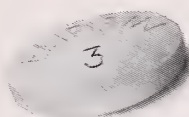
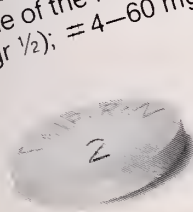
Fig. 7. Schematic diagram illustrating importance of mandible in returning the maxilla (and more superior facial structures) to its preexisting relationship with the cranial base via autorotation.

based on the structural anatomy of the face. Actually, the head can be considered as consisting of two parts: the cranium and the face. Therefore, the face

Continued on Page 159

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Vascular Thrombosis in the Upper Extremity

A Case Report Implicating a Relationship Between Trauma, Oral Contraceptives, and Smoking*

IRVING KRON, M.D., BRUCE A. MACDOUGAL, M.D., F.A.C.S.

AND JEAN J. LABELLE, M.D., F.A.C.S.**

ABSTRACT

Trauma is the most common cause of vascular thrombosis in the hand.^{1,2,3,6,8} Unfortunately, vascular thrombosis is rarely considered in the differential diagnosis of acute hand injuries. The following case report illustrates this problem in a patient who is a heavy smoker and who was taking oral contraceptives.

A heavy smoker on oral contraceptives presented with widespread vascular thrombosis in the forearm and hand six days after injury. Thrombectomy restored blood flow to all of the hand except the distal ring finger. Eight days after surgery she resumed smoking and within 24-hours rapid progression of thrombosis resulted in eventual loss of two digits.

CASE REPORT

A 40-year-old white female fell on her outstretched right hand six days prior to admission. She noted pain in her hypothenar eminence and later in her lower forearm, but paid little attention to it. One day prior to admission, she noted increased pain and coolness in her hand and came to the Maine Medical Center Emergency Room. Her hand was cool with a good radial pulse and no ulnar pulse, although an ulnar pulse was present in the left hand. X-rays of the hand were normal. The patient smoked two packs of cigarettes per day. Her only medication was Ovral[®] (Norgestrel and Ethinyl Estradiol). She returned to the Emergency Room 24-hours later. The right hand was cold and mottled with poor capillary fill. The hand had minimal motor function and decreased sensation. She had pain mostly in her little finger and ring finger. There were no palpable pulses distal to the antecubital fossa. Tenderness was elicited over the hypothenar eminence and anatomic snuff box. Doppler examination revealed no flow through radial, ulnar, or digital arteries. Transfemoral axillary angiography revealed no blood flow distal to the interosseous artery at the proximal third of the forearm (Figure 1 and 2). CBC, Prothrombin Time, PTT, platelet count, chest x-ray, and electrocardiogram were all within normal limits.

The patient was taken to the operating room. A brachial arteriotomy was done and large amounts of red thrombus and soft white thrombus were removed from the forearm but it was impossible to pass a Fogarty catheter through the palmar arches and adequate blood flow was not restored to the hand. Therefore, ulnar and radial arteriotomies were done. The vessels were catheterized and flushed with heparin and xylocaine solutions. Capillary refill returned to all but the ring finger.

Postoperatively heparin and aspirin were begun and the patient forbidden to smoke. The ring finger slowly demarcated distal to the DIP joint. On the 8th postoperative day the patient resumed smoking. The next day the level of demarcation began advancing on the ring finger. The little finger lost its capillary filling and also began demarcating (Figure 3). Multiple axillary sympathetic

blocks were performed but there was no improvement in her clinical status. The patient was discharged on the 15th postoperative day on aspirin. Four weeks later she underwent amputation of the ring finger and little fingers at the MCP joints. The patient now has a stiff, cold sensitive hand.

DISCUSSION

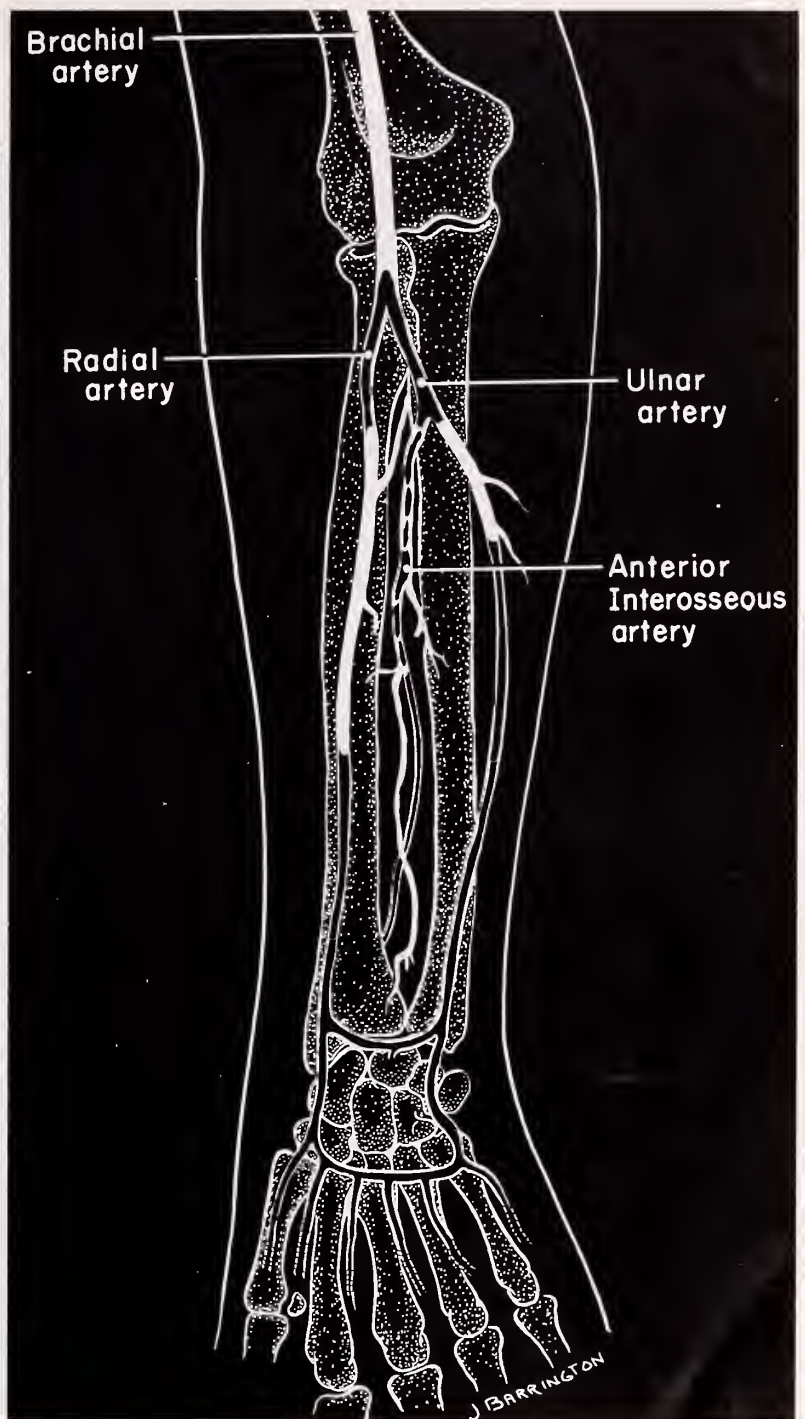
The major cause of thrombosis in the hand is repeated minor trauma although thrombosis can occur after a single injury.^{7,8,14,16,18} The ulnar artery lies just subcutaneous in the palm for a distance of about two centimeters between the hamate at the distal margin of Guyon's canal and the palmar aponeurosis. Over this distance the artery is very vulnerable to acute and chronic trauma.^{8,20} Our patient fell on an outstretched hand and there afterwards complained of persistent pain in her hypothenar eminence and later in the mid forearm.

Occlusion of the ulnar artery commonly causes Raynaud's phenomenon and can cause marked digital ischemia.^{7,18} It is rare, however, to have widespread thrombus formation in the whole forearm. The patient's smoking probably contributed to her widespread thrombosis. Nicotine, most of which is absorbed during inhalation, plays a major role by increasing peripheral vasoconstriction.^{10,11,21} Nicotine may synergistically affect the vasospasm caused by irritation of the perivascular sympathetic due to the inflammation at the thrombosed artery. Smoking also causes increased platelet adhesiveness and subsequent coagulation.^{2,9,17}

Smoking appears to have a definite relationship to occlusive vascular disease of the hand. In one series of 18 patients with ulnar artery thrombosis, all but one were smokers.¹⁶ Symptoms in patients of another series were exacerbated by smoking.⁷ Smoking had a marked effect in both digital perfusion (a rapid change shown angiographically) and digital wound healing in a patient with ulnar artery thrombosis.¹⁹ Most convincing in our patient was that after surgery she had a rapid demarcation distal to her ring finger DIP joint. The remainder of her ring finger and little finger had good capillary refill. When she began smoking on the 8th postoperative day, she very quickly lost capillary refill to both the ring and little finger. Despite a variety of medications and sympathetic blockades, she ultimately lost both the ring and the little finger at the metacarpophalangeal joint level. Oral contraceptives also have been demonstrated to increase coagulability and are also associated with increased instance of widespread thrombotic disease.^{1,5,6,22} Our case is quite similar to

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Figs. 1 and 2. The arteriogram shows a thrombus at the distal brachial artery and the proximal portions of the radial and ulnar arteries. A segment of the mid-radial artery is patent, and is probably supplied by the radial recurrent artery. There is also a patent segment of the ulnar artery, just distal to the common interosseous artery. The anterior interosseous artery is patent and supplied by collateral branches, but the posterior interosseous is occluded. There is no arterial circulation visualized distal to the forearm.

a case that Langhorne presented of spontaneous femoral occlusion which occurred in a young woman smoker on oral contraceptives. Smoking and oral contraceptives may synergistically predispose to thrombosis.¹⁵

Treatment of widespread thrombosis in the upper extremity is quite difficult. Fogarty catheterization with anticoagulation has been the standard means of

treatment.^{3,4,12,13} Recently, interarterial thrombolytic infusion has been used with excellent results when the thrombus was less than 72-hours old although poor results were obtained when the thrombus was greater than 72-hours old.¹³

Our patient's thrombosis with its sequelae of loss of two digits and cold sensitive hand may have been prevented by early recognition. History of acute



Fig. 3. This shows the hand two days after the resumption of smoking (10 days postoperatively). Prior to resumption to smoking the ring and little fingers were viable except for the ring finger tip. After resumption the ring and little fingers rapidly demarcated more proximally. Eventually both were amputated at the metacarpal phalangeal joint level.

trauma with accompanied pain in the hypothenar region, mild paresthesias, and tenderness along the ulnar artery are suggestive of the diagnosis of acute thrombosis and warrant aggressive management including arteriography if an Allen's test is positive.

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Diagnostic Imperatives In Internal Medicine

The Timely Detection of Treatable Disease

Gastrointestinal and Liver Disease

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The alimentary tract is often the seat of significant illness that is amenable to diagnosis and treatment. The gut is vascular, highly motile, and spincter bearing; it is thus easily obstructed by foreign bodies, tumors, or inflammatory illness amenable to surgical correction. The delicately integrated absorptive and neuromuscular pathways of the intestine are frequently among the first to be affected by serious endocrine, metabolic, or even psychiatric illness. The intestine is exposed to the external environment, a circumstance permitting fairly ready access to the structure and its contents. Endoscopic techniques for the purpose have become ever more sophisticated.

No sustained change in alimentary-tract function, and no persistent abdominal symptoms should be attributed to psychosomatic or emotional causes until treatable organic illness has been excluded with reasonable certainty. Successful therapy of several intestinal disorders is often accomplished by simple adjustment of diet or drugs. Malignancy of the intestinal tract, particularly of the colon, is readily detectable and potentially curable and is the second most common type of cancer in both men and women.

In the following pages, except for the liver, treatable illnesses are approached through their common presenting symptoms rather than strictly organ-by-organ.

DYSPHAGIA AND CHEST PAIN

Difficulty in swallowing is one of the most specific symptoms in all of medicine and almost always indicates the presence of organic disease. Pulmonary involvement due to aspiration is always a threat in swallowing disorders. Although the patient's perception may lead him to point directly to the site of the lesion, obstruction at the cardioesophageal junction commonly produces a sensation of dysphagia attributed to an area near the suprasternal notch.

A *foreign body in the esophagus* may go unrecognized. Children or patients with altered states of consciousness due to neurologic disorders, alcoholism or other drug ingestion, commonly forget swallowing a foreign body. A food bolus that ordinarily would not obstruct the esophagus may do so in patients with a disease reducing the size of the lumen, for example, a lower esophageal (Schatzki)

ring, esophageal stricture or carcinoma. Patients with dentures or no natural teeth are particularly prone to food obstruction; meat is a common offender. Pointed objects, such as chicken bones, are especially troublesome because they become impacted in the mucosa. Some objects are far larger than one would expect could be swallowed.

Diagnosis is suspected by history and confirmed by esophageal x-ray with barium contrast substance, and then by esophagoscopy.

Treatment of an esophageal obstruction may be complicated. It is hazardous to give food or drink in an attempt to force the object further down, as aspiration pneumonia may ensue if the patient regurgitates, but a solution of papain enzyme (such as Adolph's Meat Tenderizer) fed to the patient may successfully digest obstructing meat. Most cases, however, require endoscopic removal of the obstructing object. It is sometimes prudent not to remove an impacted foreign body, such as a chicken bone; this decision is best left to an expert. Although obstructions should not be ignored, impacted food occasionally passes through after 12 to 24 hours of waiting.

Rupture of the esophagus is a serious but uncommon cause of chest pain and may go unrecognized. It characteristically follows prolonged retching and vomiting, but such a history may not be obtained. Rarely, esophagoscopy causes esophageal perforation that is only recognized several days later as unexplained chest pain.

Diagnosis is made through the history and esophageal contrast studies. If rupture is suspected, contrast agents of the Gastrografin® type should be used for the x-rays. A surgeon should decide if and when operative correction is required; in general, rupture of the esophagus is a major emergency requiring surgery.

NAUSEA AND VOMITING

The disorders that follow are treatable conditions and should be considered in the differential diagnosis of any vomiting patients.

Poisoning or drug and alcohol intoxication are always prime suspects. The occupational history of all vomiting patients should be reviewed for exposure to industrial toxins, including inhaled substances. Many medications cause vomiting, and drug use should be reviewed in detail. There is no direct correlation between the potency and dose of a drug and

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its tendency to cause vomiting; thus, iron supplements, cold remedies, and other over-the-counter preparations may be at fault. Adulteration of food by toxic chemicals, whether by accident, through homicidal intent, or as a prank, should be considered if the history is otherwise unenlightening.

Treatment of the poisoned patient varies with the agent involved. Guidance is available from regional poison control centers and should be sought whenever doubt arises. Upper gastrointestinal symptoms, including hyperemesis gravidarum, are often the first symptom of *pregnancy*; this diagnosis should be considered in women with unexplained vomiting.

A history of eye pain, blurred vision, and haloes seen around lights suggests the diagnosis of *glaucoma* in the patient with nausea and vomiting. A tense and tender globe is further evidence and tonometry is diagnostic.

Intraabdominal infection (or a surgical abdomen) may present with nausea and vomiting in the absence of localizing symptoms and signs. The most common illnesses to manifest themselves this way are diverticulitis, cholecystitis, appendicitis, perforated peptic ulcer, renal stone, hepatitis, and infectious mononucleosis. While the last two conditions are not specifically treatable, their identification will forestall a more exhaustive workup. Elderly patients may have only nausea and vomiting as the major symptoms of serious intraabdominal disease.

A patient with nausea and vomiting may have a *bowel obstruction* at virtually any point along the gastrointestinal tract. Classical physical signs and symptoms *including* copious vomiting, a succussion splash if the gastric outlet is obstructed, abdominal pain, abdominal distension, loss of bowel sounds and reduced stool output may be present. As a rule abdominal films, one *with the patient upright* so that air-fluid levels may be seen and one with the patient supine, will be needed to confirm this diagnosis. Because intermittent, recurrent bowel obstruction may go unrecognized, any patient seen repeatedly with nausea and vomiting requires full evaluation. In the sequence of contrast studies, a barium enema should precede the upper intestinal series because surgery is hampered by barium not cleared from the upper intestine.

Recurrent pancreatitis may be caused by gallstones and they are treatable by cholecystectomy. This pancreatitis is typically indistinguishable both clinically and by serum enzyme tests from other forms, so gallstones should be sought in a patient with pancreatitis and no history of alcohol abuse. Anyone with unexplained pancreatitis should undergo an oral cholecystogram 2 to 3 weeks after the pancreatitis subsides. Successful oral cholecystography can be performed earlier if the patient is given and can tolerate a high-fat diet for two days before the study is done. Gallstones, if found, may be unrelated to the pancreatitis, but removal of the stones should be seriously considered.

Pain is also a prominent feature of acute pancrea-

titis; it is felt in the epigastrium and often in the back at the level of the first and second lumbar vertebrae. Drugs that have been incriminated in pancreatitis include the thiazide diuretics, corticosteroids, isoniazid, furosemide, azothioprine, and oral contraceptives. Rarely, the roundworm *Ascaris lumbricoides* causes pancreatitis.

ABDOMINAL PAIN

"Stomach ache" is among the most common symptoms encountered by the practitioner. It is often due to duodenal ulcer, gallstones, nonspecific intestinal infections, or bowel dysfunction. Certain less common but treatable conditions should also come to mind when patients with abdominal pain are seen.

Intoxication with heavy metals such as lead may produce chronic abdominal pain as a prominent symptom. The condition is most common in children with pica, but adults may also be affected particularly as a result of occupational exposure. The mechanism by which metal intoxication causes abdominal pain is not known. Guidance for diagnosis and appropriate therapy is available from poison control centers or local offices of the Occupational Safety and Health Administration.

Mesenteric vascular insufficiency is most common in elderly patients with chronic cardiac failure. However, younger patients with a collagen-vascular disease such as systemic vasculitis or systemic lupus erythematosus can also be affected, and oral contraceptive drugs may cause mesenteric vascular thrombosis in previously healthy women. The pain of vascular insufficiency is often severe but poorly localized and may be accentuated after eating, when the gut's demand for blood increases. Characteristically, objective physical findings are few, and because this diagnosis is difficult and testing has its risks, an experienced surgeon or internist should advise on whether or not to pursue diagnostic tests. Abdominal plain films *may* show abnormally dilated or fluid-filled loops of bowel; "thumbprinting" defects may be seen in a localized area of the bowel wall. Arteriography can be used to visualize the vessels to the gut, but even the finding of a partially or completely occluded major vessel is not proof that the patients' symptoms result from the observed obstruction, as such vessels may be found in persons having no symptoms of vascular insufficiency. All experienced vascular surgeons at one time or another have regretted operating on such patients, but surgery often is the most satisfactory approach to this difficult clinical problem.

Delayed complications of blunt trauma should be considered in a patient with vague abdominal pain. An automobile accident, a fight, occupational or sports injury can result in such serious complications as splenic hematoma, traumatic cysts of the pancreas, or rupture of the pancreatic duct, which may manifest themselves only several days after the injury.

Spontaneous peritonitis is an infection found in in-

dividuals with hepatic cirrhosis and ascites, typically in alcoholics. The offending organism is usually Gram negative, most commonly *Escherichia coli*. The means by which ascitic fluid becomes infected in these otherwise stable patients is not known. Any patient with ascites who develops abdominal pain or fever not otherwise explained should have a diagnostic paracentesis with proper examination of the fluid. The aspirate may be cloudy owing to its high content of polymorphonuclear leukocytes. The treatment is antibiotics.

Hereditary angioedema is a Mendelian dominant disorder of the complement system; affected individuals suffer intermittent attacks of abdominal pain caused by edema of the intestine. Most of them also periodically develop non-pruritic edema of the skin and mucous membranes; if the larynx becomes involved, life-threatening respiratory obstruction may occur. Rarely abdominal pain is the only complaint. The correct diagnosis is suggested by the intermittence of the attacks, which are either spontaneous or triggered by trauma; the patient has no symptoms between attacks. Serum C₁ esterase inhibitor levels are low in hereditary angioedema; a blood test for the esterase is available at most medical centers. Angioedema is treated with danazol, a testosterone derivative that increases synthesis of the inhibitor protein. For women and children, in whom androgen administration is undesirable, fibrinolytic inhibitors such as aminocaproic acid may be used for control of spontaneous attacks.

An aneurysm of the abdominal aorta or splenic artery may announce itself as abdominal pain, often in conjunction with back pain. The aneurysm is usually felt as a pulsatile mass unless the patient is obese. An x-ray showing a soft tissue mass with or without calcification supports the diagnosis; ultrasonography confirms it. Arteriography can be used to reveal extension of the aneurysm above the renal arteries or below the bifurcation of the aorta but may underestimate the size of the lesion. Aneurysms less than five centimeters in diameter rarely rupture; for larger ones, surgical resection and installation of a prosthesis is the only definitive treatment.

Ectopic pregnancy may easily be confused with gastrointestinal inflammation or such septic conditions as acute appendicitis. Pelvic examination usually reveals only diffuse tenderness. Ectopic pregnancy should be considered in any woman of childbearing age who complains of lower abdominal pain. The sudden occurrence of acute abdominal symptoms and shock in a young woman should immediately raise the suspicion of a ruptured ectopic pregnancy.

A further diagnostic consideration in the woman with lower abdominal pain, nausea, vomiting and fever is *ovarian cyst*; these lesions vary greatly in size and may twist on their pedicle to produce a clinical picture easily confused with appendicitis or ectopic pregnancy. Pain is intermittent in some patients but constant in others. The cyst is usually felt on pelvic

exam; occasionally the lesion presents as an abdominal mass first noted by the patient.

Abdominal pain is also a prominent feature of intestinal obstruction or Meckel's diverticulum, but vomiting or rectal bleeding, respectively, are more distinctive signs of these disorders.

WEIGHT LOSS, MALNUTRITION AND VITAMIN DEFICIENCY

The constellation of signs revealing inadequate nutrition is frequently encountered in chronically ill patients and in people unable to maintain adequate intake because of poverty or because they abuse alcohol or drugs. However, certain readily treatable causes of weight loss are encountered regularly by the practicing physician, and any patient with unexplained weight loss should be evaluated for the following conditions, several of which are characterized by malabsorption of dietary fat.

Ill advised low food intake is familiar to most gastroenterologists. The patient has been advised by a doctor or friend to follow a diet for the treatment of known or suspected gastrointestinal disease, but the diet may be extremely restrictive and deficient in calories. Through fear, or from simple compulsion to follow directions, the patient in time becomes malnourished. For this reason it is advisable to take a dietary history from any patient complaining of weight loss. Unless otherwise contraindicated, an adequate diet corrects the nutritional problem.

Inadequate food intake and aversion to foods enjoyed in the past is sometimes a major manifestation of *depression*, and weight loss may be extreme. Specific therapy for the nutritional deficiencies of the depressed patient is unnecessary if adequate psychiatric care is provided for the underlying illness.

Blind-loop syndrome (bacterial stasis syndrome; bacterial overgrowth syndrome) is a common and treatable complication of gastrointestinal illness; it may lead to profound malnutrition, yet the diagnosis is frequently missed because the physician doesn't think of it. Although the term "blind loop" implies that the syndrome results from surgery, it may, in fact, be caused by any of several conditions leading to stasis in the small intestine. Bacteria of fecal type then proliferate in regions where the flora is normally sparse. The most important consequence is that the bacteria degrade bile acids present in the intestinal lumen and needed for absorption of triglycerides and the fat-soluble vitamins (A, D, and K). Weight loss and then vitamin deficiencies ensue. In extreme cases, the bacteria successfully compete with their host for ingested vitamin B₁₂—to the extent that signs of megaloblastic anemia appear.

Patients who have undergone intestinal *surgery* are candidates for this syndrome, of course, particularly those who have had a Billroth II gastrectomy for peptic ulcer or a procedure leaving them with small, poorly emptying loops of bowel. But there are other common antecedents. Patients with *chronic inflammatory disease* of the intestine—typically regional

enteritis—form strictures and fistulas that encourage bacterial overgrowth. Certain *cancers*, particularly those that invade the serosa of the bowel, such as ovarian malignancies and lymphomas, are often associated with weight loss that can be explained, at least in part, by bacterial stasis syndrome. *Scleroderma*, which disrupts intestinal motility, also has this consequence, as does *diverticulosis of the jejunum*. And some patients are found to have *congenital or acquired loops* of bowel that are either blind or poorly emptying.

The diagnosis of bacterial overgrowth syndrome is made by removing upper intestinal fluid, culturing it anaerobically, and counting colonies of bacteria. Interpretation of the results should be guided by a textbook of gastroenterology. In addition, a two-stage Schilling test for Vitamin B₁₂ absorption (with and without intrinsic factor) should be performed. A barium-contrast study of the intestine to reveal dilated loops or diverticula of the jejunum is also important.

Therapy must be individualized, according to the underlying cause. Antibiotics reduce bacterial numbers and in themselves often provide for striking weight gain. Surgical correction of an obstructive neoplasm, stricture, fistula or poorly emptying afferent loop in the gastrectomized patient may eventually become necessary, although a course of antibiotics may improve symptoms to the extent that surgery is unnecessary.

Celiac disease (nontropical sprue) is a primary disorder of the small intestine, and is often responsible for severe weight loss and deficiency of fat-soluble vitamins. The protein constituent of wheat, gluten, directly or indirectly damages intestinal epithelial cells of affected individuals. Signs of the disease, in addition to weight loss, include diarrhea, steatorrhea, abdominal distension, easy bruisability, atrophy of mucous membranes, anemia, and hypocalcemia. Children under the age of ten and adults between ages 35 and 60 are most often affected. Diagnostic measures include tests of gastrointestinal absorption, x-ray of the small bowel, and peroral biopsy of the jejunum. Intestinal biopsy typically shows an absence of villi and an inflammatory infiltrate dominated by plasma cells. Because therapy is rigorous, the diagnosis of celiac disease should be firmly established before it is begun. Treatment requires removing *all* wheat from the diet. Referral of the patient to a skilled dietitian is usually necessary to insure that all wheat is excluded and to provide advice on preparing palatable meals without wheat or other products containing gluten.

Pancreatic insufficiency owing to scarring and atrophy of a repeatedly inflamed organ leads to severe malnutrition and weight loss. Pancreatitis in a setting of alcohol abuse is the most common cause of irreversible pancreatic insufficiency in North America, but some abstemious patients also suffer repeated attacks. Gallstones are a frequent cause of acute pancreatitis but rarely lead to chronic pan-

creatitis and pancreatic insufficiency. The absence of abdominal pain does not exclude recurrent pancreatitis, as patients who have experienced little or no pain during acute attacks may develop severe insufficiency of the exocrine pancreas. Although frank diabetes is a very late sequel of chronic damage, an abnormal glucose tolerance test is common by the time patients become symptomatic from malabsorption.

The basic defect is reduced output of bicarbonate and lipase by the pancreas, whereupon both hydrolysis of dietary triglyceride, for which lipase is required, and proper function of bile acids, which requires an alkaline medium, are impaired.

Pancreatic insufficiency should be suspected in patients with steatorrhea and weight loss, particularly alcoholics, who have suffered repeated attacks of abdominal pain, but pain is not an invariable symptom. Stools are often bulky and foul smelling, and oil droplets arising from the unprocessed dietary triglycerides may be seen in the toilet bowl. The abdominal plain film often shows calcification of the pancreas, and this finding is very helpful in the differential diagnosis of steatorrhea. Pancreatic cancer must also be considered in these patients and is suggested when jaundice is also present.

Malabsorption due to pancreatic insufficiency is treated with oral extracts of pancreatic enzymes needed for the hydrolysis of dietary lipid and protein. These enzymes are often most effective when accompanied with a regimen that reduces gastric acid, because they may be inactivated by low pH before they reach the small intestine. Cimetidine, a drug that reduces secretion of gastric acid by blocking the H-2 histamine receptor, is particularly effective in enhancing the benefit of pancreatic enzyme supplements. Proper treatment of chronic pancreatic insufficiency may result in dramatic weight gain.

Whipple's disease is an uncommon but treatable cause of malabsorption seen mostly in men in midlife; women are very infrequently affected. The symptoms include weight loss, steatorrhea, vitamin deficiency, arthritis, and in some patients, prominent symptoms of central nervous system dysfunction. Jejunal biopsy confirms the diagnosis if it reveals lipid-laden macrophages which stain positively in the periodic-acid-Schiff procedure. Antimicrobial agents, notably tetracyclines and ampicillin, frequently reverse the manifestations of Whipple's disease.

Other illnesses that should be considered in any patient with weight loss include *thyrotoxicosis*, *adrenal insufficiency*, *diabetes mellitus*, and *vascular insufficiency*. While each of these conditions is typically associated with other, more prominent symptoms, weight loss and malnutrition play a part in the clinical picture of many such patients.

DIARRHEA

Diarrhea is one of the most common symptoms confronting the physician in everyday practice. Most

often it is self-limited, clearing without specific therapy, but several treatable causes of acute or chronic diarrhea should be considered in evaluating these patients.

Laxative abuse may cause diarrhea that persists for months or even years. This condition is one of the most infrequently recognized causes of diarrhea, because clinicians do not consider the possibility. Failure to ask about laxative use may then lead to an unnecessary and costly evaluation. Because phenolphthalein derivatives, such as Ex-lax[®], are frequent offenders, diagnosis can sometimes be simply made by alkalinizing a specimen of stool with sodium hydroxide; a pink color is virtually diagnostic. The patient with diarrhea due to laxative abuse may have profound hypokalemia requiring urgent treatment.

Diarrhea is often caused by such *drugs* as quinidine, thyroid replacement, antacids, or antibiotics. Diarrhea is controlled by reducing the dosage or substituting an equally effective agent if one is available. Pseudomembranous colitis, a severe inflammatory complication of antibiotic administration, leads to rectal bleeding and mucous diarrhea (see chapter on Infectious Disease).

Fecal impaction in the elderly patient may paradoxically lead to diarrhea if the impaction allows only liquid to pass around it. Even younger patients, particularly those with chronic illnesses or those who are inactive because of neurologic or orthopedic conditions may develop the syndrome, as may patients who have had a barium enema. In all cases, removal of the fecal mass by enema or manual cleansing is curative.

Colo-rectal carcinoma may also cause diarrhea because only liquid is able to pass the obstructing lesion. Occult or obvious rectal bleeding is often present, but its absence does not exclude the diagnosis. The rectum must be carefully examined by finger, then by proctoscopy and barium enema to identify the lesion. Because the five-year survival of properly managed colon cancer exceeds 50 percent, this neoplasm is included here as a treatable disorder. Any patient over the age of 40 with a sustained change in bowel habits reported as unusual must be evaluated for cancer of the colon, but clearly, short-term episodes of diarrhea or constipation associated with travel, drug therapy, emotional upset, or intercurrent illness should not provoke an extensive workup.

Villous adenoma is a slowly growing, sessile tumor of the bowel that may secrete copious amounts of fluid leading to diarrhea and even to dehydration with profound hypokalemia. The surface area of such tumors is large because of the villus-like projections covering its surface. Proctoscopy or barium-contrast x-ray reveal the growth, which is surgically removed.

Diarrheogenic tumor (pancreatic cholera; WDHA* syndrome; Verner-Morrison syndrome) is a rare but treatable cause of chronic diarrhea; this pan-

creatic tumor secretes hormones that stimulate intense water and electrolyte secretion by the small bowel. The diarrhea may be continuous or intermittent but when present is of very high volume, usually more than one liter a day and often as much as five liters, and the diarrhea continues even while the patient is fasting. Dehydration, hypokalemia and abdominal cramps are common. Diagnosis is difficult, as contrast studies of the bowel, arteriography, and ultrasonography are frequently unsuccessful in locating the tumor. Although current evidence is persuasive that vasoactive-inhibitory peptide (VIP) is the responsible hormone, serum assays for VIP are not widely available and may still be misleading because many false-positive and false-negative values have been reported. Surgical exploration of the pancreas becomes necessary when clinical and laboratory values (serum, fecal, and urinary electrolytes; gastric acid levels; stool volumes, and glucose tolerance) make the diagnosis likely. In view of the complexities of diagnosis and management, the physician is advised to seek expert consultation in caring for these patients.

Not only may *thyrotoxicosis* present as chronic diarrhea but this symptom may dominate the clinical picture. Once the diagnosis is established treatment of the diarrheal state by drugs other than antithyroid medication is unnecessary.

Lactose intolerance results from deficiency of the enzyme lactase in the brush border of intestinal epithelial cells. Unabsorbed dietary lactose is osmotically active and draws fluid into the bowel lumen. Lactic acid produced from lactose by fecal bacteria contributes to the diarrhea because it inhibits absorption of water by the colon. Abdominal cramps and diarrhea rapidly follow consumption of milk or milk products by the lactase-deficient patient. Adults with no history of symptoms from milk ingestion may develop lactose intolerance. Although a lactose tolerance test is the proper way to make this diagnosis, in clinical practice removing lactose from the diet for a time often serves both for therapy and diagnosis if symptoms subside within a week. Because there is some evidence that lactase deficiency may be transitory, the physician should plan to reintroduce milk products after several months to see whether a lactose-free diet will be permanently required. As with all diet therapy of intestinal illness, a periodic review of the need for expensive or troublesome restrictions greatly benefits the patient.

Giardia and amebas cause treatable diarrhea in North America, but diagnosis is sometimes delayed for months because the parasites are not actively and expertly sought in stool samples. (see chapter on Infectious Disease).

CONSTIPATION

Although constipation from banal causes occurs often in clinical practice, four illnesses should be sought in every constipated patient before treatment is undertaken.

Constipation is a hallmark of *hypothyroidism* but

*Watery diarrhea, hypochloremia and achlorhydria

usually occurs in patients with other symptoms of thyroid insufficiency or frank myxedema. Once the diagnosis is confirmed, the constipation usually responds promptly to thyroid replacement.

Hypokalemia is frequently a cause of constipation because the ion is necessary for coordinated, propulsive motility of the colon. Constipation due to hypokalemia is typically seen in the patient on such drugs as thiazide diuretics which produce urinary loss of potassium, but any condition leading to hypokalemia may cause constipation. Restoring serum potassium to normal levels improves colon function.

The *depressed* patient often has constipation, and excessive use of laxatives to cope with this symptom is a common response to it. Constipation is relieved when the underlying affective disorder is treated.

Colorectal cancer does not as a rule cause constipation but rather a stool of decreased caliber, which the patient describes as constipation. Passage of feces is difficult and fecal volumes appears low. Most but not all patients with colorectal cancer have occult blood loss in the feces. Because bleeding may be intermittent, the patient should be given several packets for fecal smears to be obtained from bowel movements on alternate days for two weeks, and these should be returned for testing by the physician. The chance for a favorable outcome of proper therapy is such that colorectal malignancies should be approached as treatable lesions.

Constipation occurring in the course of *inflammatory bowel disease* may indicate that acute toxic dilatation of the colon is impending, as will be discussed.

ENLARGED OR DISTENDED ABDOMEN

Most patients can differentiate obesity from abdominal distension, which leads to a subjective feeling of bloating or unusual "fullness" of the abdomen after a meal. Thus, the clue to distension is predominantly a subjective sensation.

Acute toxic dilatation of the colon is a complication of inflammatory bowel disease that is a medical emergency of utmost gravity. Typically, the patient already has known ulcerative colitis and has had lapses in medical care, or has overused antidiarrheal medications. Occasionally, ulcerative colitis may present de novo with acute toxic dilatation of the colon in a previously healthy patient. Toxic dilatation is very uncommon in regional enteritis or Crohn's disease.

Fever, toxicity, and constipation accompany the abdominal distension, which is usually tympanitic. Abdominal plain film shows alarming amounts of colonic gas; the colon is dilated and its walls may be strikingly thin as reflected by loss of space between bowel loops. *Barium enema is hazardous and absolutely contraindicated* in this clinical setting.

Acute toxic dilatation is treated with corticosteroids and fluid replacement. The patient must be vigilantly observed for such signs of colonic perforation as the onset of circulatory collapse. Because the

Continued on Page 154

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CONTRAINDICATIONS Use in Newborn or Premature Infants. This drug should not be used in newborn or premature infants

Use in Nursing Mothers. Because of the higher risk of antihistamines for infants generally and for newborns and prematures in particular, antihistamine therapy is contraindicated in nursing mothers

Use in Lower Respiratory Disease. Antihistamines should NOT be used to treat lower respiratory tract symptoms including asthma

Antihistamines are also contraindicated in the following conditions: hypersensitivity to azatadine maleate and other antihistamines of similar chemical structure, monoamine oxidase inhibitor therapy (See DRUG INTERACTIONS Section).

WARNINGS Antihistamines should be used with considerable caution in patients with narrow angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy, bladder neck obstruction

Use in Children. In infants and children especially, antihistamines in overdosage may cause hallucinations, convulsions, or death

As in adults, antihistamines may diminish mental alertness in children. In the young child, particularly, they may produce excitation

OPTIMINE TABLETS ARE NOT INTENDED FOR USE IN CHILDREN UNDER 12 YEARS OF AGE

Use in Pregnancy. Experience with this drug in pregnant women is inadequate to determine whether there exists a potential for harm to the developing fetus

Use with CNS Depressants. Azatadine maleate has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc.)

Use in Activities Requiring Mental Alertness. Patients should be warned about engaging in activities requiring mental alertness, such as driving a car or operating appliances, machinery, etc.

Use in the Elderly (approximately 60 years or older). Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients

PRECAUTIONS Azatadine maleate has an atropine-like action and, therefore, should be used with caution in patients with a history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, hypertension

DRUG INTERACTIONS MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines.

ADVERSE REACTIONS The most frequent adverse reactions are underlined

General: Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose, and throat.

Cardiovascular System: Hypotension, headache, palpitations, tachycardia, extrasystoles.

Hematologic System. Hemolytic anemia, thrombocytopenia, agranulocytosis

Nervous System Sedation sleepiness dizziness disturbed coordination fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesias, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions

Gastrointestinal System Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.

Genitourinary System: Urinary frequency, difficult urination, urinary retention, early menses

Respiratory System Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness

OVERDOSAGE Antihistamine overdosage reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms (dry mouth, fixed, dilated pupils, flushing, and gastrointestinal symptoms) may also occur

If vomiting has not occurred spontaneously, the patient should be induced to vomit. This is best done by having him drink a glass of water or milk after which he should be made to gag. Precautions against aspiration must be taken, especially in infants and children

If vomiting is unsuccessful, gastric lavage is indicated within three hours after ingestion and even later if large amounts of milk or cream were given beforehand. Isotonic and 1/2 isotonic saline is the lavage solution of choice

Saline cathartics, such as milk of magnesia, draw water into the bowel by osmosis and therefore are valuable for their action in rapid dilution of bowel content

Stimulants should not be used.

Vasopressors may be used to treat hypotension

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mortality from this disorder is as high as 50 percent, total colectomy should be considered if it persists more than twenty-four hours. The physician and surgeon must agree whether to remove the colon and when. This decision is always difficult.

The patient with a distended abdomen secondary to *bowel obstruction* usually has abdominal pain, vomiting and constipation; but elements of this triad may be absent.

GASTROINTESTINAL BLEEDING

The sudden onset of gross upper or lower gastrointestinal bleeding is a dramatic clinical event that should set into motion a well-defined sequence of diagnostic measures. Many intestinal illnesses may be responsible for bleeding; certain less common, or frequently overlooked, causes will be emphasized here.

HEMATEMESIS

Vomiting of blood in adults can be attributed, in 90 percent of cases, to bleeding peptic ulcers of the stomach and duodenum, acute erosive gastritis, or esophageal varices. Less common causes are peptic esophagitis, gastric polyps, or benign tumors of the stomach and upper small intestine.

Despite its frequency, *gastritis* occasionally does not appear in the differential diagnosis because some physicians associate it primarily with alcohol abuse. But gastritis leading to significant and even massive upper gastrointestinal hemorrhage can also be seen in patients receiving such drugs as aspirin (or one of the many over-the-counter drugs containing aspirin), non-steroidal anti-inflammatory agents, or broad spectrum antibiotics, among others. Thus, a careful history of drug ingestion must be included in the initial workup of a patient vomiting blood.

The *Mallory-Weiss syndrome*, bleeding tears in the upper stomach or lower esophagus, may occur in patients who suffer repeated retching and vomiting, or who abruptly vomit a large volume of gastric contents. The mucosal rent usually affects the gastric mucosa high in the fundus, and the lesion may or may not cross the cardioesophageal junction. Bleeding may be massive, although spontaneous cessation is the rule in patients with normal coagulation. However, Mallory-Weiss tears are often seen in alcoholics whose liver disease may cause disorders of clotting that prolong the bleeding. Endoscopy confirms the diagnosis, and surgical correction is needed if bleeding is severe or prolonged.

Aorto-duodenal fistula is an uncommon complication of aortic aneurysm, which causes forceful hemorrhage that may prove treatable if surgical care is immediately available. It is not widely recognized that this condition may be preceded by several weeks of occult gastrointestinal bleeding.

RECTAL BLEEDING (MELENA)

The sudden passage of either bright red blood or black stools has many causes. The most common are

hemorrhoids, diverticulosis, tumors, bacterial dysentery, and all the causes of upper intestinal bleeding discussed earlier. The following brief list includes only conditions that are not widely recognized causes of rectal bleeding and are amenable to definitive therapy.

The color of the stool may be helpful in locating the lesion. Bright red blood typically arises from lesions distal to the splenic flexure, "burgundy" colored stools from the more proximal colon or distal ileum, and black stools from lesions in the stomach and small intestine.

Meckel's diverticula are discrete lesions found in the caudal half of the small intestine. Because the diverticula may contain gastric mucosa secreting acid and pepsin, they are subject to ulceration and bleeding. Young patients, typically between the ages of 15 and 35, with recurrent melena but otherwise in good health are the most likely candidates for this disorder; however, a Meckel's diverticulum may only become troublesome in later life.

The stool usually is burgundy colored, consistent with the location of the lesions. Barium-contrast study of the small intestine demonstrates the diverticulum in lateral views, which place the lesion in profile. The radiologist should know that Meckel's diverticulum is a possibility because radiologic demonstration is often difficult. Technetium-99m is concentrated by gastric mucosa and thus may be helpful in finding the lesion. If bleeding is brisk and active, arteriography frequently discloses the site of hemorrhage. Yet surgical exploration for a diverticulum may be necessary even without confirmatory radiologic findings.

Aortoenteric fistula causes a dramatic and life-threatening intestinal hemorrhage, which may produce melena without hematemesis, often after a period of occult bleeding. The only treatment is repair of the aneurysm.

Angiodysplasia of the colon, local vascular lesions revealed by high-quality arteriography, are surprisingly frequent causes of rectal bleeding in patients over the age of forty. The lesions, appearing in the distal small intestine and ascending colon, are noninflammatory dilatations of venules and capillaries. Because of the clinical observation that angiodysplasia and aortic stenosis occasionally coexist, it has been postulated that poor bowel perfusion from any cause may lead to these vascular shunts. Diagnosis requires arteriography with magnification techniques. Surgical resection of the affected bowel segment is required. The resected colon may appear grossly normal to a pathologist, because the lesions collapse when emptied of blood.

Brisk rectal bleeding, usually bright red and mixed with mucus, can occur in patients with either *ulcerative colitis* or *regional enteritis*, and either disorder, especially ulcerative colitis, may present itself with rectal bleeding in the absence of diarrhea, cramps, or its other common features. Proctoscopy reveals the inflamed mucosa of ulcerative colitis,

usually with shallow, small ulcerations that may appear less hemorrhagic than expected from the vigor of the bleeding episode. Bleeding is less frequent in regional enteritis and proctoscopy may reveal no gross mucosal abnormality because this condition often spares the rectum. Barium enema is needed for the diagnosis, but barium studies in the acute phase of suspected inflammatory bowel disease should be very cautiously considered. Abdominal plain films may demonstrate "thumbprinting" defects in the wall of the colon or small intestine if there is enough intestinal air to allow proper contrast.

A *foreign body in the rectum* may cause bleeding. A careful and complete history is obviously necessary for diagnosis, and abdominal plain films with special views of the pelvic area may reveal a radio-opaque object. Because bleeding indicates that the object may be embedded in the mucosa, skill is required in manipulating and removing it to avoid the serious complication of perforating the rectum or sigmoid colon.

Although *anal fissure* is readily visible when the anal sphincter is carefully examined, bleeding fissures are frequently overlooked. Because the bleeding is bright red, it appears more profuse to the patient than it really is. The anus must be inspected with a gentle but firm spreading of the anal margins to efface the spincteric folds that otherwise may obscure the cleft-like lesion. Local heat (sitz baths) and soothing suppositories to treat the fissure should be accompanied by an attempt to regulate bowel habits and prevent recurrence. Recurrent or stubbornly persistent perianal inflammation may signify underlying regional enteritis.

Mesenteric vascular insufficiency may announce itself with black or burgundy-colored stools, when other typical symptoms of this illness, abdominal pain and cramps, are inconspicuous or absent. Episodes of mesenteric vascular ischemia are common in older people, especially those with congestive heart failure or other circulatory disorders, and patients with collagen diseases, such as lupus erythematosus and vasculitis. The use of oral contraceptive agents may be complicated by mesenteric thrombosis.

Occult gastrointestinal bleeding—the "guaiac positive" stool—results from slow or intermittent blood loss at any site in the gastrointestinal tract. If bleeding is intermittent it may only be detected in smears obtained by the patient from a series of stools passed on alternate days. Occasionally, a diet high in meat products may produce false-positive stools, which become negative on a meat-free diet. The gastrointestinal tract of a "guaiac positive" patient should be completely examined and the presence of hemorrhoids or other minor lesions should not distract the physician from seeking a more serious cause.

Many treatable illnesses of the alimentary tract give rise to occult bleeding, neoplasms prominently among them. Colorectal malignancies have a rela-

tively high probability of cure if detected early; screening stool for occult blood is the simplest way to accomplish this. Benign tumors and vascular malformations are the other *treatable* lesions most likely to account for continuous or intermittent occult loss of blood. Duodenal ulcer very infrequently gives rise to slow bleeding (if it bleeds it does so abundantly); so a guaiac-positive stool should not be attributed to a duodenal ulcer or deformed bulb seen radiologically. On the other hand, such common conditions as peptic esophagitis, *gastric* ulcer, and diverticula of the colon can ooze slowly, giving rise to stools positive for occult blood.

THE LIVER

The treatable causes of liver disease commonly lead to one of three presentations: enlargement, jaundice, or "hepatitis" (abdominal pain, anorexia, nausea, vomiting, and jaundice).

Liver enlargement is recognized when the organ becomes palpable, although a normal liver may be felt at or just below the costal margin. By percussion, the normal adult liver should not exceed about 12 cm in vertical dimension. Of the many causes of hepatomegaly, only a few are significantly affected by prompt treatment.

Fatty liver from chronic, excessive intake of alcohol can occur in any heavy drinker. Fatty liver does not, in itself, lead to cirrhosis. The treatment is simply abstinence, which allows the liver to reduce in size, sometimes within a week. If the liver does not shrink—and the patient is in fact abstinent—other causes of the swelling should be sought.

The normal liver has a nearly unlimited capacity to store vitamin A; so that the chronic, heavy ingestion of the vitamin, though rare in itself, can produce hepatomegaly. With cessation of intake, the liver slowly returns to normal size.

Heart disease, notable deformity of the tricuspid valve, constrictive pericarditis, or congenital defects, should be considered in any child or adult with hepatomegaly. Passive congestion produces a painlessly enlarged liver but some tenderness may be observed on physical examination. Hepatojugular reflux is also observed, and pulsus paradoxus, if present, suggests pericardial constriction, which can be confirmed by cardiac fluoroscopy or ultrasound. Treatment is directed to the cardiac condition.

Adenomas of the liver, exceedingly rare before the advent of oral contraceptives, are occurring with markedly increased frequency, presumably owing to widespread use of the "pill." These tumors should be suspected in any woman with hepatomegaly or abnormal liver function who is taking contraceptive medication. Radioisotope scanning or computerized tomography should demonstrate the lesions. Although histologically benign, they may cause pain, perhaps as they bleed into the liver substance, or they may hemorrhage into the peritoneum. For this reason, it is currently thought advisable to remove large, easily palpable lesions, though withholding

contraceptives often causes pronounced shrinking of the tumors.

Of the many causes of *jaundice*, medical or surgical, three noninfectious processes require urgent diagnosis so that appropriate therapy can be introduced. Common-duct obstruction by a gallstone, if untreated, may lead to serious infection of the biliary tree and then septicemia with gram negative organisms. Gallstones are very common in the general North American population, but they occur even more frequently in women taking oral contraceptives, patients on cholesterol-lowering drugs, descendants of certain American Indian tribes, and patients whose red-cell survival is shortened, as in hereditary spherocytosis, thalassemia major, and cirrhosis of the liver. The typical history is of longstanding, vague pain, which may be epigastric, in the right upper quadrant, or scapula; it is usually intermittent. Eventually severe pain, dark urine and jaundice ensue. But in some cases symptoms may be much more subtle; mild abdominal discomfort, or none at all, may be reported. As is the case with many illnesses, elderly patients are likely to present with atypical signs and symptoms. A common duct stone, whether still present or recently passed, often produces symptoms that are easily confused with those of hepatitis.

After a careful history and physical examination, tests for liver function and contrast studies of the gallbladder and bile duct are performed. Ultrasound techniques have recently proved valuable in detecting gallstones, particularly in jaundiced patients when cholecystography is unsatisfactory. Occasionally, a radio-opaque gallstone may be identified on a plain film of the abdomen.

Gallstones causing jaundice must be surgically removed. At this writing, gallstone-dissolving drugs, such as chenodeoxycholic acid, have no place in the therapy of symptomatic gallstone disease.

The jaundiced patient should be carefully questioned regarding medications, including those used within the past few months but recently stopped, as drug jaundice may occur even after a medication has been discontinued. Anesthetics, particularly of the halothane class, should also be considered. Although certain drugs are much more likely than others to cause jaundice, isolated case reports indicate that any drug may be responsible for jaundice in an individual susceptible to it. Both diagnosis and therapy of drug-related jaundice require withdrawal of the suspected medication. The patient should be carefully followed to confirm the relief of jaundice and to exclude other causes of liver or biliary tract disease.

Rarely, jaundice occurs in a patient undergoing hemolysis, although red cell destruction must be acute and severe to cause significant rises in serum bilirubin. Diagnosis is straightforward: anemia, reticulocytosis, and high serum bilirubin with an elevation of the unconjugated (indirectly-reacting) fraction are the hallmarks. The underlying hemolytic disorder must be treated.

The complex of *abdominal pain, vomiting,*

anorexia, and *jaundice* is seen with sufficient frequency to merit special discussion. Several treatable illnesses cause the "hepatitis," and differentiating among them tests the physician's diagnostic skills. Drug hepatitis and cholangitis are relatively common causes. A search for extrahepatic obstruction of the bile ducts should be made if "hepatitis" is encountered in a patient who is unusually ill, is known to have gallstones or suspected to, has fever or shaking chills (both uncommon in viral hepatitis), or is elderly, in which case gallbladder disease may present a confusing clinical picture.

Wilson's disease is an inherited disorder of copper metabolism that damages both liver and central nervous system by depositing of copper in them. Symptoms appear in childhood or adolescence. Infrequently, Wilson's disease will become clinically manifest as late as the second or third decade with a dominant hepatitis-like clinical picture. Recently, patients with Wilson's disease have been described with a clinical picture easily mistaken for the chronic active hepatitis that follows viral infection of the liver. Unexplained neurologic or neuro-psychiatric disorders in the hepatitis patient *or members of his family* should raise the question of Wilson's disease. Suspicion becomes stronger if serum ceruloplasmin levels are below normal, assuming that gastrointestinal or renal loss of plasma protein is not occurring. Urinary and hepatic tissue copper assays confirm the diagnosis, as do greenish-brown Kayser-Fleischer rings found in the corneal limbus. The copper-chelating drug penicillamine is effective in Wilson's disease if the disease is recognized and treated before changes are irreversible.

Chronic active hepatitis (chronic aggressive hepatitis) is a sequel of viral hepatitis occurring in 1 to 2 percent of patients who have the acute illness. Despite much current research, it is not known why some patients with acute viral hepatitis go on to develop chronic active hepatitis. If the condition is recognized before irreversible post-necrotic cirrhosis occurs, patients can be successfully treated with corticosteroids. Chronic active hepatitis should be suspected in the following settings:

- a) After acute hepatitis, liver-function tests do not return completely to normal within three months.
- b) The hepatitis occurred in a setting of intravenous use of illicit drugs.
- c) Unexplained abnormalities in liver-function tests, hepatomegaly, or splenomegaly are found even with no history of acute hepatitis.
- d) In the course of hepatitis or in the convalescent months such signs of cirrhosis as spider teleangiectasias, gynecomastia, ascites, persistent itching, or longstanding anorexia appear.

The diagnosis of chronic active hepatitis should be confirmed by percutaneous needle biopsy of the

Continued on Page 159

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From the Secretary's Notebook

Summary of Proceedings, Interim Meeting, M.M.A. House of Delegates, March 22, 1980 in Waterville, Maine

The Interim Meeting of the M.M.A. House of Delegates was held at the Mid-Maine Medical Center in Waterville on Saturday, March 22, 1980 with an attendance of 51 delegates and alternates. Brinton T. Darlington, M.D., President of the M.M.A., called the meeting to order and George W. Bostwick, M.D., Speaker of the House, presided.

1. Reports of Officers—Dr. Darlington reported on the need for adequate time for the public and physicians to study the SHCC Preliminary State Health Plan and proposed the following resolution from the Executive Committee: "That a Committee be empowered to review all options, including the necessity of seeking injunctive relief, concurrent with the review procedure, including contact with other associations." This resolution was *approved unanimously* by the House.

Dr. Darlington did point out to the House that initial legal costs would be approximately \$800. He asked that each county medical society see that someone in each county analyze the Plan to see how it's going to directly affect health care of their patients, and that they join forces with others in their county (hospitals, etc.) to see what, if any, action they want to take.

2. Financial Statement of Income and Expenditures for 1979 and Budget Proposed for 1981 was presented by Dr. Richard Leck, Chairman of the Budget Committee. Final action on the proposed budget for 1981 will take place at the annual meeting of the House of Delegates on June 12 and 13, 1980 at The Balsams in Dixville Notch, NH.

3. The preliminary report of the Committee on Nominations (printed) was given to each delegate. The report consisted of nominees for vacancies on the standing committees, for President-elect, and for each position to be filled on the Executive Committee (this year, Androscoggin, Hancock, Lincoln-Sagadahoc, Knox, Oxford, Penobscot, Piscataquis, Somerset and Waldo counties). Final vote will be at the annual meeting of the House of Delegates in June. **A brief biographical sketch on each officer nominee** was sent to members of the House of Delegates.

4. Committee report:

a) *M.M.A. Health Insurance Plan*—Dr. Michael Rynne, Chairman, reported on his committee's findings thus far, and expects to report back in June with

specific plans from different insurance companies. In the meantime, he recommends signing the current BC/BS contract as it now stands with no increase in premiums. He noted that it is reviewable every 90 days.

5. Dr. Bostwick announced members who will serve on **Reference Committees** during the Annual Session in June.

6. Resolutions—Six resolutions were presented to the delegates (copies sent to all delegates on 3/12/80), and five of them will be referred to the June 1980 meeting of the House of Delegates for action. The following resolution, submitted by the Androscoggin County Medical Association, was *unanimously approved* and was referred to the Peer Review Committee for study and report to the House in June:

WHEREAS: PSRO had not clearly shown the medical community or the Department of Health Education and Welfare that utilization review improves the quality of medical care or reduces its cost; and

WHEREAS: The Pine Tree Organization of Maine freely calls itself a physicians' organization; and

WHEREAS: The staff of the Pine Tree Organization consists of no actively practicing physicians; and

WHEREAS: The Board of Directors of the Pine Tree Organization of Maine has members from the insurance industry and the Maine Department of Human Services; and

WHEREAS: Through recent arrangements with Blue Cross/Blue Shield of Maine and the Department of Human Services, the Pine Tree Organization of Maine is rapidly developing into an enforcement and penalizing organization;

THEREFORE BE IT RESOLVED: That the President and Executive Committee of the Maine Medical Association be instructed to develop a study group to determine whether the Maine Medical Association should continue its endorsement of the Pine Tree Organization of Maine and that the findings of the study group be presented for a vote of the House of Delegates of the Maine Medical Association at its annual meeting in June 1980.

7. Old Business—

a) Dr. Robert McAfee, A.M.A. Delegate, discussed two items that have been previously sent to the delegates: A.M.A.'s **UU Report on Chiropractic**, and Dr. Todd's Report on Revision of **A.M.A. Prin-**

ciples of Medical Ethics. Dr. McAfee asked that the delegates be prepared to discuss these issues at length at the June meeting in order that he may receive direction before the A.M.A.'s annual meeting in July.

b) Dr. Francis Kittredge, member of the Board of the **Joint Underwriting Association**, reported that they recently met and felt that it was impractical to continue as they are insuring only 83 physicians at the present time. The Board is looking into phasing the JUA out in the near future.

8. Adjourned at 4:25 P.M.

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“INSIDE-OUT AND BOTTOM-UP”—A Philosophy of Facial Reconstruction Revisited

Continued from Page 142

can be thought of as a separate entity, merely suspended from anterior and below the cranial base (Figure 1 and 2). The mandible, or lower jaw, is the formidable bone of the face, and it represents the foundation upon which the rest of the face is rebuilt. Once reconstructed it reestablishes the anterior-posterior position of the entire face by defining the position of the original occlusion (Figure 4 and 5). The occlusion relates the maxilla to the reconstructed mandible, as well as reapproximates the bony fractures to near normal position. The only key to the return of the maxilla to its preexisting relationship with the cranial base is by allowing the mandible to direct it to this position.² Thus, the vertical dimension of the face is predicated on the exact reconstruction of the facial bones from bottom-up, followed by autorotation of the mandible (Figure 7). If one were to start reduction at the orbits and work downward, the fractured segments (being eggshell in consistency) “could easily be incorrectly positioned and malalignment would be so magnified at the level of the dental occlusion that it would be impossible to establish a functionally correct intermaxillary relationship.”³

SUMMARY

“Inside-out and bottom-up” is an organizational

approach in the treatment of maxillofacial injuries. For those surgeons who treat facial injuries, it dictates the treatment sequence to be followed in the treatment plan. For those who are not involved in the treatment of the entire maxillofacial injury, but rather limit their field of expertise to a specific organ or structure making up part of the face, it establishes guidelines as to when in the sequence of events reconstruction of that part of the face should commence. If one follows the treatment sequence “inside-out and bottom-up,” satisfactory and rewarding reconstruction of the face will result.

ACKNOWLEDGEMENT

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DIAGNOSTIC IMPERATIVES IN INTERNAL MEDICINE—Continued from Page 156

liver; therapy with steroids should not be instituted without a tissue diagnosis, and Wilson's disease should first be ruled out. It must be emphasized that

an antecedent history of acute hepatitis may not be obtained from these patients, as the initial infection may have been subclinical.

Necrologies

ALBERT S. CRAWFORD, M.D.

1887-1979

Dr. Albert S. Crawford, 92, of Laguna Hills, California, died on October 8, 1979.

Born in Hermosillo, Sonora, Mexico on March 4, 1887, he was the son of Mathew and Harriet Crawford.

Dr. Crawford was graduated from Pomona College, received his medical degree from Cornell University College of Medicine in 1915, interned at Lane Hospital in San Francisco and served a residency at the New Haven General Hospital in Connecticut. He took postgraduate courses at the Mayo Clinic and Yale-in-China College of Medicine in China.

He was an Associate Professor of Surgery and Neurosurgeon at

the University of Wisconsin from 1925-1926, Neurosurgeon at Henry Ford Hospital in Detroit from 1926-1952, Thayer Hospital in Waterville from 1953-1955 and at the Veterans Administration Center in Togus from 1955-1963. Dr. Crawford was also associated with the Mt. Desert Hospital in Bar Harbor and the Ellsworth General Hospital.

An honorary member of the Kennebec County Medical Association and the Maine Medical Association, he received a 50-year pin in 1965, a 55-year pin in 1970 and a 60-year pin in 1975. He was also a member of the American Board of Neurology and Neurological Surgery.

LOUIS A. ASALI, M.D.

1909-1979

Dr. Louis A. Asali, 69, of Scarborough, Maine, died on November 20, 1979.

Born in Portland, Maine on December 8, 1909, he was the son of Andrew and Agelina S. Asali.

Dr. Asali was graduated from the University of Maine and received his medical degree from Tufts University School of Medicine in 1935. He interned at the Maine General Hospital in Portland and served a residency in Surgery at Bellevue Hospital.

In 1937, he located in Scarborough where he was affiliated with the Mercy Hospital and the Maine Medical Center in Portland.

During World War II, he served in the U.S. Army Medical Corps as a Captain.

Dr. Asali was a member of the Cumberland County Medical Society and the Maine Medical Association.

Surviving is his widow, the former Audrey A. Leavitt.

WALTER H. SIELING, JR., M.D.

1914-1979

Dr. Walter H. Sieling, Jr., 65, of Stuart, Florida, died on November 28, 1979.

He was born on April 2, 1914, the son of Walter H. and Lilian O. Sieling.

Dr. Sieling was graduated from New York University and received his medical degree from State University of New York College of Medicine, Brooklyn in 1943.

Following his internship in Lucas City, Toledo, Ohio, he entered the U.S. Army, serving from November 1944-December 1968,

holding the rank of Major. Specializing in Internal Medicine, Dr. Sieling practiced in Stony Brook, New York and was affiliated with the John T. Mather Memorial Hospital in Port Jefferson, New York. He located in Bristol, Maine in 1969 and in 1973 moved to Stuart, Florida.

He was an affiliate member of the Cumberland County Medical Society, the Maine Medical Association and the American Medical Association.

RICHARD P. LANEY, M.D.

1907-1980

Dr. Richard P. Laney, 72, of Skowhegan, Maine, died at a local hospital on January 20, 1980.

Born in Skowhegan, Maine on April 5, 1907, he was the son of William J. and Louise M. Laney.

Dr. Laney was graduated from Bowdoin College and received his medical degree from Hahnemann Medical College and Hospital in 1932. Following an internship at Crozier Hospital in Chester, Pennsylvania and a residency at Memorial Hospital in Worcester, Massachusetts, he spent a year in practice in Brunswick and another year in Norridgewock before returning to his home town.

During World War II, he was a clinical pathologist for the 16th General Hospital, a 1,000-bed tented hospital. Discharged with the rank of Lieutenant Colonel, Dr. Laney returned to Skowhegan and with his newly-acquired experience in hematology and cardiology, helped organize a medical laboratory at the local hospital.

Dr. Laney was a senior member of the Somerset County Medical Society and the Maine Medical Association. He served as Councilor for the Fourth District of the M.M.A. from 1954-1956, Alternate Delegate to the A.M.A. from 1969-1974, was chairman of the Scientific and Peer Review Committees of the M.M.A., past president of the American Society of Internal Medicine and honorary member of Medical Records Committee of the Redington-Fairview General Hospital. He also was a recipient of the Maine Blue Cross and Blue Shield "Award of Appreciation" and the A.H. Robins' Physician Award for Community Service.

Surviving are his widow, the former Marion M. Rock; one son, William of Skowhegan; three daughters, Mrs. William Reed of Orono, Mrs. Peter Seamans of Portuguese Bend, California and Mrs. Wellington Gordon of Quantico, Virginia; one sister, Mrs. Joseph Cayoutte of Skowhegan; and eight grandchildren.



CONTINUING MEDICAL EDUCATION IN MAINE

Conferences and Workshops

Title: Maine Medical Association's Annual Scientific Session
Date: June 14, 15, 1980
Location: The Balsams, Dixville Notch, New Hampshire
Sponsor: Maine Medical Association
Credit: AMA and LCCME Category I
For further information contact Patricia Bergeron, Maine Medical Association; 622-3374.

Title: Seminar on Sports Medicine
Date: June 30-July 3, 1980
Location: Bowdoin College, Brunswick
Sponsors: Regional Memorial Hospital and Bowdoin College
Credit: AMA and LCCME Category I—20 hours
Reg. Fee: Tuition \$240

For further information contact Office of Continuing Medical Education, Regional Memorial Hospital; 729-0181 Ext. 206.

Title: Family Medicine Update
Date: September 7-10, 1980
Location: Spruce Point Inn, Boothbay Harbor
Sponsors: AAFP and Medical Care Development
Credit: AMA and LCCME Category I—15 hours and AAFP (prescribed)—14 hours

Reg. Fee: \$150; \$120 for State of Maine AAFP members
For further information contact Gerald Goold, Medical Care Development; 622-7566.

Title: Tri-State Surgical Association Annual Meeting
Date: November 6-9, 1980
Location: Castle Harbor Hotel, Bermuda
Sponsor: Maine Chapter, American College of Surgeons
Credit: AMA and LCCME Category I—18 hours
Reg. Fee: None

For further information contact John Towne, M.D.; 872-7713.

PROGRAMS SPONSORED BY MID-MAINE MEDICAL CENTER/COLBY COLLEGE

Title: Obstetrics and Gynecology
Date: July 7-11, 1980
Credit: AMA and LCCME Category I; AAFP—18 hours

Title: Pediatrics
Date: July 14-18, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—16 hours

Title: Surgical Techniques
Date: July 15-18, 1980
Credit: AMA and LCCME Category I—16 hours

Title: Dermatology for the Non-Dermatologist
Date: July 24-28, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—16 hours

Title: Neurosurgical Techniques
Date: July 27-30, 1980

Credit: AMA and LCCME Category I—21 hours
Title: Otolaryngology
Date: August 3-7, 1980
Credit: AMA and LCCME Category I—18 hours
Title: Epilepsy
Date: August 5-8, 1980
Credit: AMA and LCCME Category I; AAFP—18 hours
Title: Ophthalmology
Date: August 10-14, 1980
Credit: AMA and LCCME Category I—18 hours

Title: Nuclear Medicine
Date: August 17-21, 1980
Credit: AMA and LCCME Category I—28 hours
Title: Medical and Surgical Emergencies
Date: August 19-22, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—25 hours

Title: Forensic Science
Date: August 24-27, 1980
Sponsors: In cooperation with the National Association of Medical Examiners

Credit: AMA and LCCME Category I; AAFP—24 hours
Title: Pulmonary Disease
Date: August 24-28, 1980
Credit: AMA and LCCME Category I—21 hours

All of the Colby activities will be based at the Colby College campus in Waterville. Registration fee is to be determined. For further information contact Robert Kany, Ph.D., Colby College; 873-1131 Ext. 267/251.

Hospital Activities

Augusta General Hospital Augusta, Maine

May 27, 1980
7:30-8:30 a.m.
Pediatrics—Blood Gases
George Little, M.D., Dartmouth Medical School
This program has been certified AMA and LCCME Category I and AAFP (prescribed). For further information contact Mrs. Nancy Favorite; 623-4711. This program may be viewed over ITS.

Augusta Mental Health Institute Augusta, Maine

May 22, 1980
10-11:30 a.m.
Issac Ray—Maine Physician
Jacques M. Quen, M.D., Professor of Psychiatry, Department of Psychiatry School of Medicine, Cornell University, Ithaca, New York.
This program has been certified AMA and LCCME Category I. For further information contact Ulrich Jacobsohn, M.D.; 622-3751 Ext. 243.

Central Maine Medical Center Lewiston, Maine

May 21, 1980
Mid-Trimester Abortion

12 Noon	Mark Levine, M.D., Central Maine Medical Center	
June 18, 1980	Perinatal Morbidity and Mortality	
12 Noon	Case discussions	
Every Thurs.	Tumor Board	12-1 p.m.
Every Friday	Medical Grand Rounds	9-10 a.m.
4th Friday (Odd Months)	Joint Surgical Grand Rounds	7:45-8:45 a.m.
2nd Fridays	Visiting Professorship, Boston University	1-3 p.m.

All activities have been certified AMA and LCCME Category I. For further information contact Carol Murrell, Central Maine Medical Center; 795-2435.

Eastern Maine Medical Center Bangor, Maine

May 22, 1980	Visiting Professor Day in Orthopedics	
10 a.m.-3 p.m.	Arthur E. Ellison, M.D., Williamstown, Massachusetts	
Every Mon.	EEG Conference	12-1 p.m.
Every Mon.	Surgical Service—Chief's Rounds	5-6 p.m.
4th Mon.	ENT Section Meeting	12-1 p.m.
4th Mon.	Neurosurgery Section Meetings	4-5 p.m.
3rd Tues.	Dermatology-Pathology Conference	5-6 p.m.
3rd Tues.	Dermatology Section Meeting	6-7 p.m.
4th Tues.	Pulmonary Medicine Section Meeting	8-9 a.m.
1st Wed.	Hematology/Oncology Meeting	8-9 a.m.
Every Wed.	Tumor Clinic Conference	2-5 p.m.
Every Wed.	Radiology Conference	5-6 p.m.
	(1) Ultrasound/Nuclear Medicine	
	(2) Radiology Film Review	
	(3) Neuroradiology	
	(4) Teaching File Conference	
	(5) G.I. Radiology	
1st Thurs.	Ophthalmology Section Meeting	7:30-8:30 a.m.
	OB-GYN Conference	8-9 a.m.
	(1) Pathology	
	(2) GYN Analysis	
	(3) OB-Pediatric Combined	
	(4) In-Service and Education	
Every Thurs.	Pediatric Grand Rounds	9-10 a.m.
Every Thurs.	Medical Service Conference	10-11 a.m.
Every Thurs.	Cardiology Conference	11 a.m.-1 p.m.
2nd Thurs.	Orthopedic Grand Rounds	7:45-8:45 a.m.
4th Thurs.	Orthopedic Service Meeting	7:30-9 a.m.
4th Thurs.	Surgical Service Death Review	7:45-8:45 a.m.
Every Thurs.	Psychiatric Service Grand Rounds	10-11 a.m.
4th Thurs.	Urology Section Conference	7:30-8:30 a.m.
Every Fri.	Neurology Grand Rounds	8-9 a.m.

Visiting Professor Program:

2nd Thurs.	Medical Service Visiting Professor	10 a.m.-5 p.m.
2nd Thurs.	Anesthesia Service Visiting Professor	7-8 a.m.
3rd Thurs.	OB/GYN Serv. Visit. Professor	10 a.m.-4 p.m.
Saturdays	Surgery Service Visiting Professor	8 a.m.-Noon
4th Thurs.	Pediatric Service Visiting Professor	10 a.m.-5 p.m.
as scheduled	Orthopedic Service Visiting Professor	
as scheduled	Family Practice Visiting Professor	
as scheduled	Psychiatric Service Visiting Professor	

All activities have been certified AMA and LCCME Category I. For further information contact James F. Lawsing, III, M.D., Coordinator, Medical Education Committee; 947-3711 Ext. 2303.

Henrietta D. Goodall Hospital Sanford, Maine

May 20, 1980	Drug Therapy 1980	
7 p.m.	Darrell R. Abernethy, M.D., Ph.D., Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts	
This meeting will be held at the Henrietta D. Goodall Hospital's Conference Room. This program has been certified AMA and LCCME Category I and AAFP (prescribed). For further information contact Melvin Bacon, M.D.; 324-3632.		

A. R. Gould Memorial Hospital Presque Isle, Maine

Every Thurs.	Tumor Conference	
8 a.m.		
2nd Thurs.	Perinatal Conference	
11:30 p.m.		
1st & 3rd Fri.	Tumor Conference	

The tumor conferences will be held in the Rotary Regional Educational Center and the perinatal conference will be held in Conference Room A. These conferences have been certified AMA and LCCME Category I. For further information contact Marilyn Dean; 769-2511.

Maine Medical Center Portland, Maine

Every Mon.	Student Technologist Conference	8 a.m.
Every Mon.	Hematology-Pathology Conference	11 a.m.
Every Mon.	Pulmonary Conference	12 Noon
Every Mon.	Pediatric Residents' Conference	1 p.m.
Every Mon.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Mon.	Surgical Pathology Review	4 p.m.
Every Mon.	Radiology Journal Club	5 p.m.
1st & 3rd Mon.	Clinical Nephrology Conference	11 a.m.
1st & 3rd Mon.	Hematology-Pathology Conference	12 Noon
3rd Mon.	Eye Conference	11:45 a.m.
Every Tues.	Radiology Residents' Seminar	7 a.m.
Every Tues.	Family Practice Grand Rounds	9 a.m.
Every Tues.	Electrocardiographic Interpretation	1 p.m.
Every Tues.	Psychiatric Grand Rounds	1:30 p.m.
Every Tues.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Tues.	Surgical Seminar	4 p.m.
Every Tues.	Pathology Slide Seminar	4 p.m.
1st & 3rd Tues.	Radiology-Pathology Conference	12 Noon
1st & 4th Tues.	Neurology Conference	12 Noon
2nd Tues.	Infectious Disease Conference	12 Noon
3rd Tues.	Hematology Conference	12 Noon
5th Tues.	Oncology Conference	12 Noon
Every Wed.	Radiation Therapy Conference	7 a.m.
Every Wed.	Urology Conference	7 a.m.
Every Wed.	Student Technologist Conference	8 a.m.
Every Wed.	Continuing Education Seminar	8 a.m.
Every Wed.	Medical Conference	9 a.m.
Every Wed.	Psychiatric Journal Club	12 Noon
Every Wed.	Cardiology Seminar	12 Noon
Every Wed.	Surgical Grand Rounds	5 p.m.
2nd Wed.	Guest Internist—Medical Conference	9 a.m.
4th Wed.	Medical Mortality Conference	9 a.m.

Alt. Wed.	Neurology-Psychiatry Seminar	11 a.m.
Alt. Wed.	Anesthesiology Journal Club	3 p.m.
Every Thurs.	Thoracic Surgery Conference	7 a.m.
Every Thurs.	OB/GYN Conference	7 a.m.
Every Thurs.	Anesthesiology Clinical Conference	7 a.m.
Every Thurs.	Diagnostic Radiology Teaching Conf.	7 a.m.
Every Thurs.	Surgical Conference	8 a.m.
Every Thurs.	Pediatric Conference	9 a.m.
Every Thurs.	Tumor Consultation Board	11 a.m.
Every Thurs.	Medical Residents' Conference	12 Noon
Every Thurs.	Surgical Seminar	4 p.m.
Every Thurs.	Endocrinology Conference	5 p.m.
Every Thurs.	Dental Specialty Lecture	6 p.m.
1st Thurs.	Anesthesia Mortality Conference	7 a.m.
1st Thurs.	Guest Pediatrician	9 a.m.
1st Thurs.	Gastroenterology Conference	12 Noon
1st, 3rd Thurs.	Cardiac-Surgical Conference	12:30 p.m.
1st, 3rd, & 5th Thurs.	Pulmonary-Physiology Conference	12:30 p.m.
2nd Thurs.	Cardiology Teaching Conference	12:30 p.m.
2nd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
2nd Thurs.	Eye Staff Scientific Session	5:30 p.m.
2nd Thurs.	Maine Medical Center Medical Staff Meeting and Scientific Session	6 p.m.
2nd & 4th Thurs.	Pulmonary-Pathology Conference	12 Noon
2nd & 4th Thurs.	Endocrinology Conference	12 Noon
3rd Thurs.	Combined Guest Physician or Guest Surgeon Program	8 a.m.
3rd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
4th Thurs.	Surgical Mortality Conference	8 a.m.
4th Thurs.	Anesthesia Mortality Conference	3:30 p.m.
Last Thurs.	Pediatric Mortality Conference	9 a.m.
Every Fri.	Thoracic-Surgical Conference	7 a.m.
Every Fri.	Nuclear Medicine Conference	7 a.m.
Every Fri.	Student Technologist Conference	8 a.m.
Every Fri.	Neurological-Neurosurgical Conference	8:30 a.m.
Every Fri.	Gastroenterology Conference	9 a.m.
Every Fri.	Medical Rehabilitation Staff Conf.	9 a.m.
Every Fri.	Orthopedic Conference	9 a.m.
1st Fri.	Dermatology Conference	12 Noon
2nd Fri.	Nephrology Conference	12 Noon
3rd Fri.	Rheumatology Conference	12 Noon
4th Fri.	Oncology Conference	12 Noon
Alt. Fri.	Oncology Radiation Conference	7 a.m.
Alt. Fri.	Gastroenterology Conference	10 a.m.

All programs have been certified AMA and LCCME Category I. For further information contact Costas T. Lambrew, M.D.; 871-2111.

Penobscot Bay Medical Center Rockland, Maine

May 23, 1980	Surgical Grand Rounds
May 30, 1980	Family Practice Grand Rounds
June 6, 1980	Orthopedic Grand Rounds
June 13, 1980	Medical Grand Rounds
June 27, 1980	Surgical Grand Rounds

These grand rounds are from 11 a.m. to 12 Noon and have been certified AMA and LCCME Category I. For further information contact Lloyd Roberts, M.D.; 594-9511.

St. Mary's General Hospital Lewiston, Maine

Every Tues. 8-9 a.m.	Medical Grand Rounds
1st & 3rd Fridays 12-1 p.m.	Tumor Conference
Last Fri. of month 12-1 p.m.	Surgical Grand Rounds

The Surgical Grand Rounds will be alternating monthly between St. Mary's General Hospital and Central Maine Medical Center. These activities have been certified AMA and LCCME Category I. For further information contact Michael C. Bach, M.D.; 783-2227.

V. A. Hospital Togus, Maine

June 20, 1980 10 a.m.	Therapeutic Approaches to Neuropathies Marilyn R. Kassirer, M.D., Staff Neurologist, Veterans Administration OutPatient Clinic, Boston VA Hospital.
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Every Wed. 1:15-2:15 p.m.	Medical Staff Service Meetings
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Every other Thurs. 2-3 p.m.	Oncology Clinic
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2nd Tues. of month	Psychiatric CME Meetings
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These activities have been certified AMA and LCCME Category I. For further information contact E. Osborne Coates, Jr., M.D., VAM and ROC, Togus; 623-8411

ANNOUNCEMENT: Medical Care Development, Inc. is now receiving a listing of continuing medical education activities taking place in Vermont, New Hampshire, and Massachusetts. If you wish further information contact Gerald Goold, Medical Care Development; 622-7566.

Annual Meeting Dates For Your 1980 Calendar...

Maine Medical Association, June 12-15
The Balsams, Dixville Notch, New Hampshire

American Medical Association, July 20-24
Downtown Chicago Marriott, Chicago

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Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported, should these occur, discontinue drug. Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long-term therapy.

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County Society Notes

Knox

The Knox County Medical Society met at the Sail Loft Restaurant in Rockport on March 4, 1980 at 6:30 p.m. with eleven members present.

Old business: Dr. Ted Schettler was voted into membership in the Knox County Medical Society. Membership requested the secretary send a letter of thanks to Senator Sam Collins for his efforts on behalf of passage of LD 1906.

New business: President requested all members to consider the questionnaire sent out by the secretary very seriously. The questionnaire regarded input as far as priorities for the long-range plan for Maine Medical Association activities. The secretary will compile responses and return them to the Executive Director of Maine Medical Association. It was emphasized that members be specific and spend some time considering the various activities because it is their dues dollars which pay for the activities of the Maine Medical Association.

Following dinner, Dr. Peter Shrier discussed the recent and past history and current status of the Health Care Finance Committee negotiations with Blue Shield. The membership voted unanimously to express their thanks to Dr. Peter Shrier for his efforts on behalf of the Maine Medical Association.

There being no further business, the meeting was adjourned at 9:30 p.m.

ALBERT J. LANTINEN, JR., M.D., Secretary

Washington

A regular meeting of the Washington County Medical Society was held on March 18, 1980 at the Staff Room of the Down East Community Hospital in Machias with thirteen members and guests present.

Meeting initially presided over by Dr. Karl V. Larson, Secretary, in the absence of Dr. James C. Bates, President.

I. Mr. Guy B. Seaberg, Assistant Attorney General Chief of Medicaid Fraud Control Unit, was unable to attend due to illness.

II. Dr. Toby W. Acheson of Machias was elected Vice President, following which he chaired the meeting.

III. Dr. Donald M. Robertson of Harrington, Executive Committee Representative from Washington County, presented matters that had been taken up in the Executive Committee meetings.

a) The fact that Blue Cross will not pay for consultations, unless a copy of the consultation is presented to them. The members of the Society did not look with much favor on this suggestion.

b) The next item brought up for discussion by Dr. Robertson was the Preliminary Report of the State Health Plan of Maine, a 400-odd page product of HSA and the Bureau of Health with the main discussion being the affect upon the smaller hospitals. This plan will favor centralization and the reduction in size of smaller hospitals and perhaps eventually phasing out many of their services, especially obstetrics. This particular plan released by the Dept. of Human Services was released only March 4, 1980 following a three (3) year study and there was only one week between the release of the document and the hearings. Because of the size of the report, it was impossible to study it adequately before the hearings. Since each State must submit its health plan by April 1, 1980, there has been no opportunity for the medical profession and the general public to peruse this plan and see how it affects various parts of the State in regard to medical services. Members of the Society were asked to telegraph Gov. Joseph Brennan, requesting that pressure be placed on HEW, to extend the deadline for 90 days, in order to allow adequate dissemination of the information.

Dr. Harold V. Gaskill, Jr. commented on the plan and how it would affect, directly, Down East Community Hospital, with the loss of four (4) obstetrical beds and two (2) of M&S beds; total of six (6) beds and further destroy the effectiveness of the hospital, as a complete unit.

Dr. Robert G. MacBride, a member of the HSA, also com-

Continued on Page 194

Information for Authors

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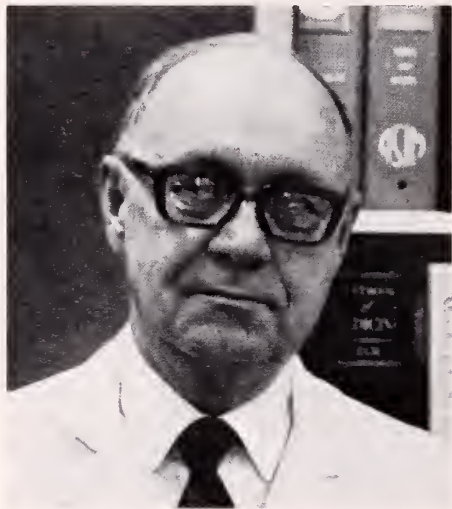
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Unusual Complications Following Abdominal Hysterectomy: Dyspareunia and Consort Glans Laceration After Vaginal Cuff Stapling

JOHN ZERNER, M.D., FACOG, FACS,* BUELL A. MILLER, M.D., FACOG*
AND BRUCE D. NELSON, M.D., FACS*

Stapling instruments and techniques have been available for several years with increasing acceptance in gastrointestinal, thoracic and vascular surgery. In gynecologic surgery, these techniques were first applied for abdominal and vaginal hysterectomies as well as colpoplastic procedures. Initial reports mentioned no coital problems. However, dyspareunia in two patients following the placement of vaginal cuff staples has been reported.⁶

Recent evaluation of a patient complaining of severe dyspareunia and whose consort experienced post coital glans irritation demonstrated that staples closure of the vaginal cuff with subsequent migration and partial opening of the staples seemed to be the cause of these complaints. We now wish to discuss and comment upon this unique situation.

CASE REPORT

J.T., a 35-year-old white divorced gravida VII, para VII was admitted to MMC on 5/17/76, approximately nine months following TAH, LSO and appendectomy performed at another institution. Initial surgery (9/23/75) had included the use of staples on the pedicles as well as closure of the vaginal cuff. Following this surgery, the patient complained of increasing leukorrhea, dyspareunia, and post coital bleeding. When first seen by one of the authors (BAM) four months following initial surgery, induration and tenderness were noted at the vaginal cuff. Numerous staples were removed vaginally at that time and also on two other occasions. However, not only did symptoms persist but bladder discomfort ensued, necessitating urologic consult. An IVP showed no urinary abnormality; these films, however, demonstrated a clip present at the vaginal apex (Figure 1). Cystoscopic examination

was performed and considered to be within normal limits. Fluoroscopic studies were also obtained. A metal clamp placed at the vaginal cuff localized the remaining clip in what appeared to be a submucosal location (Figure 2). Severe discomfort continued unabated with dyspareunia to such a degree as to prevent normal coitus. Additionally, patient's consort described glans bleeding post coitally.

On 5/18/76, an examination under anesthesia using radiographic studies for further localization was performed. The offending clip was identified; incision was made at the vaginal cuff and this foreign body removed. Since then, coitus has been normal for both the patient and her consort. No further dyspareunia has occurred.

DISCUSSION

First use of metal staples in abdominal surgery occurred in 1908. Technique developed by Hult⁹ was cumbersome and thus not widely adopted. Refinement of the procedure took place at the Research Institute of Experimental Surgical Apparatus and Instruments in Moscow² and then was applied extensively for gastric resection⁴ and rectal anastomosis³ in the U.S.S.R. Steichen,⁷ working in New York City, adopted auto stapling for gastrointestinal, thoracic and vascular surgery. This has been increasingly utilized over the ensuing years by American surgeons.

Kahn⁵ first introduced auto suturing for gynecologic procedures in abdominal hysterectomy. Metal staples were placed on all pedicles with a double row of staples placed across the vault of the vagina. No serious immediate or delayed complications were reported in a series of twenty-two patients. No coital problems were noted either in the patients nor in their consorts. In 1971, Albert¹ described the use of staples for vaginal hysterectomy and col-

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Fig. 1. IVP study demonstrating partially opened vaginal staple. (1) The pedicles show placement of staples in these areas (2) and (3).



Fig. 2. Fluoroscopic study using Allis clamp (1) localizing staple in an apparent submucosal location.

poplasties. A total of eleven vaginal hysterectomies and thirteen colpoplastic procedures were listed. His report stated that most of these staples were buried in the healing process and thus would not be a source of trouble. However, many staples needed to be removed from the vaginal cuff two to three weeks after surgery, with an average of five to seven staples being removed per patient. One patient required local anesthesia for staple removal secondary to severe pain. All patients were allowed coitus six weeks after surgery. No coital discomfort had been noted nor did their male partners experience any coital difficulty.

In 1977, Messitt⁶ described two cases of dyspareunia following placement of auto suture staples at the vaginal cuff during abdominal hysterectomy. Both patients had excision of the vaginal apex with removal of these wire sutures under general anesthesia. Complete relief of symptoms was noted in both individuals. In neither case had mention been made of consort discomfort or laceration. Messitt felt strongly that metal sutures caused an irritating focus in the sensitive apex of the vaginal vault thus resulting in dyspareunia and urinary problems. He further suggested a long-term study to evaluate the use of staples for closure of the vagina in order to ascertain the true incidence of these problems.

In our patient (J.T.), description of dyspareunia and post coital bleeding along with consort glans irritation and bleeding marked the first time these symptoms had been noted to occur simultaneously in the female and male partner following auto suturing of the vaginal cuff.

Placement of auto sutures on supporting ligaments or at an anastomotic line has an excellent hemostatic effect; some migration, however, has been described at variable times following application. No episodes of bowel or urinary perforation have occurred to date although this might occur if metal sutures are not properly set with good approximation of their edges. Goligher² mentioned that following bowel anastomosis, staples had been noted by rectal palpation to be extruded to the intestinal lumen over a period of months.

The vaginal cuff presents a unique situation due to the mobility of the vaginal tissue and the chance of trauma at the cuff during coitus. Thus, metal staples may work loose from their original application and migrate to other areas.⁷ Albert¹ has described spontaneous expulsion and also the need for removal of metallic clips from the vaginal cuff over a period of time. Hence, in our patient, it is acceptable to theorize that coitus itself loosened the clips, allowing the ends to separate and then cause trauma not only to the vaginal tissue but also to the glans of her consort's penis. The suppliers of the staples state the possibility of vaginal or penile discomfort during intercourse is minimal.⁸ However, they have emphasized that in performing anterior and/or posterior colporrhaphy use of auto sutures should not be used in individuals coitally active because of the possibility of trauma as the staples are fully exposed in the vagina.

We would state therefore that in those patients planning future coitus it be advised that permanent metallic closure using either wire or staples be considered inappropriate thereby avoiding the dyspareunia, bleeding and potential consort discomfort that has been described. Additional office procedures, the possibility of hospitalization with anesthesia and surgery, all of which increase mental and physical trauma to the patient, can then be avoided.

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The Diagnostic Imaging Dilemma

ALFRED E. SWETT, M.D.*

As all physicians know, new problems are constantly arising in the practice of medicine. As a radiologist, I feel that a particular situation is of sufficient importance to merit public discussion. In recent times, astute clinicians have been heard mumbling phrases such as photon deficiency, image enhancement and humbug. On occasion, they have been overheard asking questions of radiologists. Questions like: What the devil do we do next? Where do I start? What, no barium enema?

The reason for this problem is a literal upheaval in the traditional methods of diagnostic imaging. Rapid technological advances in nuclear medicine, computed tomography, ultra sonography and special procedures have given us an array of alternatives with which to effectively make diagnoses in most clinical settings.

The basic tools of diagnosis, the clinical history and physical examination remain paramount. Diagnostic imaging procedures are after all an extension of the physical examination which further localize and characterize the pathology as to organ system, body cavity or region. In order to appropriately and effectively make decisions as to the best imaging study, the results and findings of the referring physician's history and physical must be available to radiologists. These images are a literal extension of the clinician's hands and eyes.

The problem which has arisen is the lack of pertinent clinical history and physical findings when one is presented with an unknown patient who needs a proper diagnostic workup. A few years ago, before the availability of these multiple methods of examination, a rather simple diagnostic protocol was well known to all clinicians and radiologists. Today this is not true. Radiologists have had to make an intense effort to keep abreast of the "state of the art" in nuclear medicine, computed tomography and ultra sonography. It is not surprising that physicians in clinical medicine are sometimes confused and traumatized when a radiologist suggests a different approach such as ultra sonography or nuclear medicine as being more appropriate for a specific patient.

Within recent years numerous papers have appeared in the literature, presenting the relative merits and disadvantages of ultrasound, computerized tomography, radionuclide scanning and diagnostic radiology. Whalen¹ presents an excellent summary of his experience. In a teaching institution, standard flow sheets outlining the diagnostic workings of a specific clinical problem such as renal masses can be formulated. These are an excellent teaching process but should not lead to cookbook medicine.

The effectiveness of a given procedure is determined by many factors. In hospitals of less than major medical center size, not all methods will be available. In larger institutions, the relative merits of one method versus another are determined by the interest and experience of physicians involved, the state of development of the equipment used and the technical competence available. Therefore, the recommendations for the best imaging study may not be the same in different institutions.

A somewhat different approach to the same problem is presented by Shuman and Hellman.² Their proposal that the radiologist act as a clinical consultant is a logical attempt to correlate the knowledge and expertise of the referring physician and the radiologist. This thrusts the radiologist into the clinical setting to a greater extent than most radiologists have previously known. It calls for closer cooperation between the referring physician and radiologist than we have heretofore experienced and makes it mandatory that the radiologist be informed as to the current clinical status of a given patient.

In a department where residency programs exist, a senior radiology resident may function in the capacity of consultant. In other departments, a specific radiologist with knowledge of the methods available may function in this role. Reaction to the Vermont program has been not entirely favorable. It is understandable that some specialties feel threatened by the intrusion of diagnostic imaging into their heretofore well defined specialty areas. This is particularly noted in the procedure oriented subspecialties. The prime motivation for choosing the right diagnostic approach is to enable us to implement correct therapy, be it surgical or medical and to keep the diagnostic workup as cost effective as possible. Another important consideration is the reduction of the radiation dose to the patient. This is of major importance in the female of childbearing age as well in the entire pediatric population. The correct examinations need to be properly performed in a properly prepared patient and in the right sequence.

The best solution is an ongoing program of education and dialogue between all referring physicians and radiologists. The evaluation of the imaging methods available in a given institution and in a patient with a given clinical picture can be properly made only if both the radiologist and the clinician are fully aware of these and make the study a cooperative venture. If, for whatever reason, this does not occur the quality and cost of care will be much jeopardized. The pathway which will insure appropriate examinations is simple. It is open communications between the physicians involved. Truly a simple solution which we all should support fully.

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A Case of Campylobacter Fetus Septicemia in Maine

MARGARET OSTRANDER, B.A., MT (ASCP)* AND JOHN D. RICE, JR., M.D.**

CASE REPORT

A seventy-six-year old white man was admitted to Mercy Hospital complaining of pain in the left lower quadrant and shortness of breath of about one week duration. Physical examination showed the patient to have a pulse rate of 162, blood pressure of 160/90 and a temperature of 38°C. The lungs were clear; ear, nose and throat examination was normal except that poor dental hygiene was noted. Mild tenderness was present in the left lower quadrant. A chest x-ray was considered to be within normal limits. Electrocardiograms indicated atrial flutter and some sub-endocardial injury. Laboratory findings included: a WBC of 13,900; with 66 percent polymorphonuclear leukocytes; 31 percent bands; 2 percent lymphocytes; 1 percent monocytes. The hematocrit was 35.3. Stool was guaiac positive. The patient was admitted for treatment of atrial arrhythmia and for evaluation of fever, ischemia, left lower quadrant pain and guaiac positive stool.

During his hospitalization, the patient was treated successfully for the atrial flutter with Inderal® and digoxin. As there was no obvious source for the fever, two blood cultures were drawn. The patient was started on intravenous ampicillin, 1 gm. initially and 500 mg. every six hours. During the next few days, the patient experienced fever up to 39°C, but by the end of the first week his temperature returned to normal.

On the fourth hospital day, faintly staining Gram negative spiral shaped organisms were isolated from both blood cultures. The organisms grew aerobically with 5% CO₂, and anaerobically. Due to the morphology and the darting, corkscrew-like motility of the organism, it was thought that these could be spirochetes of some kind. However, there was no clinical evidence to support a diagnosis of rat bite fever or relapsing fever. The patient, insofar as is known, kept no pets and had no significant contact with animals outside his house.

Subcultures of the organism recovered from the blood were forwarded to the Maine State Public Health Laboratory, and a tentative diagnosis of *Treponema macrodentium* was made. It was then decided that the patient's septicemia was possibly a result of his extremely poor dental health. Subcultures were then sent to the Center for Disease Control in Atlanta, Georgia. There the organism was identified as *Campylobacter fetus*, subspecies *intestinalis*.

Although previous clinical studies have shown that the symptoms of *C. fetus* infections are extremely variable, fever, abdominal pain and diarrhea are considered to be classical symptoms of *C. fetus* ss *intestinalis* bacteremia.¹ In retrospect, it appears that this patient had two of the three "classical" symptoms, i.e., fever and abdominal pain. The misidentification of the organism as spirochetes, which they closely resemble morphologically, prevented the correct diagnosis of the patient's illness.

Until recently, *Campylobacter fetus* has been considered to be an animal pathogen, causing septic abortion in ungulates, enteritis in poultry and diarrhea in calves and puppies.²

The first reported human infection was the description of abortion in an infected woman in 1947.³ Since then *C. fetus* has been implicated in enteritis,^{1,4,5} bacteremia,¹ pulmonary abscess and empyema,⁶ phlebitis, arthritis, meningitis,¹ and

TABLE I

Characteristic	IDENTIFICATION OF SUBSPECIES OF CAMPYLOBACTER FETUS ⁸		
	Subspecies		
	<i>Fetus</i>	<i>Intestinalis</i>	<i>Jejuni</i>
H ₂ S (TSI or SIM)	—	—	—
H ₂ S (Lead Acetate)	—	+	+
Growth in Brucella Broth plus 1% Glycine	—	+	+
Growth in Brucella Broth plus 3.5% NaCl	—	—	—
Growth at 25°C (Brucella Broth)	+	+	—
Growth at 42°C (Brucella Broth)	—	—	+

Reiter's syndrome.⁷ There are three recognized species of *C. fetus*: *jejuni*, *intestinalis* and *fetus*. The subspecies *jejuni* and *intestinalis* are responsible for disease in humans, while *C. fetus* ss *fetus* has only been isolated from animals.⁸

The route and source of infection in man are not completely understood. Individuals with no exposure to farm animals have been infected. Recent outbreaks of *Campylobacter* enteritis suggest an enteric route of infection.^{1,4,8} In most cases, no obvious source of infection can be identified.⁹ It is common for one or more predisposing factors for infection to be present, such as immunosuppressive therapy, alcoholism, cardiac disease or hepatorenal disorders. There is a tendency for adults to be infected with *C. fetus* ss *intestinalis*, while most isolates from children are subspecies *jejuni*.¹

During the last year, there have been two reported outbreaks of gastroenteritis due to *C. fetus*. One occurred in Vermont in 1978, and was thought to be the result of a contaminated public water supply.¹⁰ The other was a report of enteritis in a household in Colorado in March and April 1979. A total of seven persons and a puppy became ill and it is not known whether the household members were infected by the puppy or whether they all acquired the infection from an unknown common source.¹¹ The isolates in both cases were *C. fetus* ss *jejuni*. There was also a report of *C. fetus* infection in people who consumed raw milk. This outbreak occurred in Los Angeles County in November 1976.¹²

Campylobacter fetus is a slender curved Gram negative rod which may appear comma or "S" shaped. Loosely wound spiral filaments up to 8 millimicra in length are seen in old cultures. They are actively motile with a darting, corkscrew-like motion.¹³ *Campylobacter* are microaerophilic, requir-

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ing 5% CO₂ for growth. Most isolates will also grow under anaerobic conditions.

Selective media have been formulated for the isolation of *C. fetus ss jejuni* from feces.^{8,14} The organism described in this report was isolated initially from Trypticase Soy Broth (Difco) which had been inoculated with 10 cc of blood from the patient, and incubated at 37°C. both aerobically and anaerobically. At 48 hours the organism appeared as pinpoint colonies on chocolate agar incubated with 5-10% CO₂. It also grew anaerobically on Trypticase Soy Agar with 5% sheep blood.

Criteria for the differentiation of *Campylobacter* subspecies are presented in Table 1.⁸

Although at one time *Campylobacter fetus* was thought to be an infrequent cause of human disease, it is being isolated with increasing frequency, particularly as a cause of bacteremia and enteritis.

This paper represents what may be the first reported case of *Campylobacter* related illness in Maine. As laboratories and physicians become more familiar with the organism, no doubt more cases will be encountered in the future. *Campylobacter* infection should be considered when spirochete-like forms are isolated in cases of septicemia.

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Diagnostic Imperatives in Internal Medicine

The Timely Detection of Treatable Disease

Infectious Diseases

MICHAEL BARZA, M.D.*

INTRODUCTION

Infectious diseases are prime examples of diagnostic imperatives. Of the vast number of treatable ones, I have selected for discussion primarily those which may be diagnostically elusive and potentially life-threatening. Some are quite uncommon, but most are liable to be seen by any busy practitioner. The diseases in this chapter are arranged as a series of syndromes; for example, bacteremia, pneumonia, diarrhea, or hepatitis, because this is the manner in which they are viewed by the physician.

The general principles and the rationale of therapy have been outlined in some detail. However, I have avoided explicit therapeutic recommendations except where there is general agreement on a particular regimen or where new information is available that might not be found in standard textbooks. In emphasizing the necessity for surgical intervention in many of these disorders, I am acknowledging the fact that the activities of the infectious disease practitioner and of the surgeon often lie remarkably parallel.

BACTEREMIA

Diagnosis:

Bacteremia should be suspected in any acutely febrile patient. The temperature elevation may be blunted in individuals who are old, debilitated, or receiving corticosteroids. The finding of a polymorphonuclear leukocytosis or "shift to the left" in the peripheral blood smear is helpful in preliminary differentiation from viral infection. The history, physical examination, chest x-ray and urinalysis generally provide a strong indication of the probable portal of entry. However, the *biliary tract*, *colonic diverticula*, and female *genitourinary tract* may be extremely subtle sources of infection. Repeated physical examinations together with appropriate radiographic studies will usually lead to the correct diagnosis.

Foci of *suppurative phlebitis*, occurring where intravascular devices have been in place for prolonged periods, may likewise easily be missed. The physician must have a high index of suspicion for thrombosed veins in the upper extremities. If aspiration of these sites yields pus, they should be excised surgically. Infection of larger veins, for example, subclavian

vessels which have been the site of central lines, may be inferred from the clinical setting and demonstration of thrombosis on venography. In addition to antibiotics, anticoagulant therapy may be necessary in order to prevent embolism from large veins.

Patients who are *severely leukopenic* or have other major *defects in their resistance to infection* often have bacteremia without an apparent source. Small breaks in the skin or mucous membranes appear to afford access to microorganisms in these cases.

When a previously healthy individual exhibits signs of bacteremia with no apparent portal of entry, *bacterial endocarditis* or more rarely *typhoid fever* should be suspected. Infective endocarditis is discussed later in this chapter. Additional clues to typhoid fever are abdominal symptoms, constipation, relative bradycardia, and a "cloudy" sensorium. Evanescent macules on the trunk, so-called "rose spots", are seen in some patients with this disease.

Blood cultures are the cornerstone of diagnosis in suspected bacteremia. The results not only prove the diagnosis but often point to the likely source. In addition to obtaining several blood cultures, the physician should take additional steps when the possibility of bacteremia is raised. If *skin lesions* are found, they should be aspirated for gram-stained smear and culture. If fungal infection, vasculitis, or tumor is a reasonable possibility such lesions should be biopsied. *Metastatic foci*, for example, a septic arthritis or pleural empyema, should be aspirated in order to obtain fluid for gram-stain and culture. If *gonococcemia* is a consideration, swabs of the cervix and anus should be cultured on Thayer-Martin medium. If *typhoid fever* is suspected, stool should be cultured. Unfortunately, the Widal test for salmonellosis is rarely useful because of the high rate of false-positive results.

Approach to therapy:

Table 1 shows some suggested regimens for the initial therapy of suspected bacteremia. Clearly, there is considerable overlap among the various combinations and a number of other therapeutic approaches could readily be substituted for those shown. Penicillins should, of course, be avoided in the *penicillin-allergic patient* and, if the allergy is known to be severe such as giant urticaria or anaphylaxis, cephalosporins should be avoided as well. The dosages indicated in the footnote are only rough guidelines and should be adjusted for the state of

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renal and hepatic function. If there is evidence of central nervous system involvement, a *lumbar puncture* should be done. It must be remembered that *cephalosporins*, *clindamycin*, and *aminoglycosides* do not penetrate the meninges adequately for most therapeutic purposes after systemic administration. Although there is a certain amount of interchangeability among classes of drugs, e.g., nafcillin and oxacillin, carbenicillin and ticarcillin, gentamicin and tobramycin, there are occasional advantages of one congener over another even at the initial stages of therapy. For example, nafcillin is preferred over oxacillin or cephalosporins for acute bacterial endocarditis because of its greater synergy against the enterococcus. As soon as the infecting organism is identified, the regimen should be modified appropriately.

Complications:

The premonitory signs of *bacteremic shock* may be subtle. They include *hypotension*, *confusion*, and *oliguria*. If intravenous fluids together with appropriate antibiotic therapy fail to restore the circulation promptly, a bolus of *steroids*, for example, methylprednisolone 30 mg/kg, should be given.¹ This dose may be repeated after several hours if the response is poor or transient.

In addition to shock, other consequences of bacteremia include metastatic infection, disseminated intravascular coagulation, and "shock" lung ("adult respiratory distress syndrome"). *Metastatic infection* is usually signaled by local signs and symptoms in the area which has been secondarily seeded. However, if this focus is endovascular, e.g., on the heart valves or endothelial surface of arteries, it may be missed. Non-typhoidal salmonellas such as choleraesuis or typhimurium show a curious tendency to *colonize atherosclerotic aneurysms* of the distal aorta or its branches. This should be suspected when salmonella bacteremia fails to respond or recurs despite adequate therapy.² Pain may be present in such aneurysms and there may be contiguous osteomyelitis. Without surgical excision, the aneurysm may rupture fatally. Occasionally, other species of bacteria may infect arterial aneurysms.³

Of considerable interest is the recent demonstration that patients with *Streptococcus bovis* bacteremia have an exceedingly high rate of underlying intestinal lesions including colonic carcinoma in about half, as well as other colonic, gastric, or esophageal lesions.⁴ These individuals merit thorough studies for the possibility of such lesions even in the absence of gastrointestinal signs or symptoms or stools positive for occult blood.

Disease Mimicking Septicemia:

Some non-infectious illnesses may mimic bacterial septicemia. These include acute hematologic disorders such as leukemia, collagen-vascular disease such as systemic lupus erythematosus, and allergic reactions. Occasionally, thyrotoxicosis, acute adrenal insufficiency, or pheochromocytoma may be

confused with infection.⁵ These entities can usually be readily excluded by the history, physical examination, and appropriate laboratory tests of thyroid and adrenal function as well as catecholamine excretion.

BACTERIAL ENDOCARDITIS

Diagnosis:

The triad of *fever*, *anemia*, and a *heart murmur*, point to the diagnosis of infective endocarditis. Fever with *stroke*, and fever with *unexplained renal insufficiency* should also raise the possibility of this disease. A murmur is not invariable, particularly in the early phases of acute bacterial endocarditis in which this sign may be absent in one-third of cases.

The diagnosis is made by blood cultures, which are positive in over 90% of cases. Six blood cultures should be obtained over a period of at least several hours. Factors that may contribute to make these cultures negative include: recent antibiotic therapy; right-sided valvular infection; disease due to pyridoxine-requiring streptococci;⁶ and fungal endocarditis. If possible, blood cultures should be obtained after the patient has been without antibiotics for 48 hours. Right-sided valvular infection is suggested by the occurrence of pulmonary emboli and is especially common in abusers of intravenous drugs. Special media are available for pyridoxine-requiring streptococci. Fungal endocarditis usually occurs in immunosuppressed patients. The vegetations are often large and detectable by ultrasound; emboli to major vessels are common and fungal elements can be seen if such emboli are excised.

Atrial myxoma may present a clinical picture not unlike that of bacterial endocarditis. It is usually readily diagnosed by cardiac ultrasound.

Treatment:

There is generally an opportunity to await the reports of positive blood cultures before starting therapy for suspected subacute bacterial endocarditis. In contrast, acute endocarditis, suggested by the sudden onset of hectic fevers and chills, evidence of metastatic lesions to lungs, musculoskeletal system or elsewhere, or known intravenous drug abuse, is an urgent matter. Antibiotics should be instituted as soon as blood cultures have been drawn. Therapy should be directed at gram-positive cocci, particularly *Staphylococcus aureus* and the enterococcus. Gram-negative bacilli, especially *Pseudomonas aeruginosa* are a major problem in drug addicts. Nafcillin and an aminoglycoside provide excellent initial coverage for these organisms (Table 1).

Complications:

A variety of complications may occur in the course of treated or untreated endocarditis. These are of two major types: (1) those due to progression of the local infection, producing valvular insufficiency and congestive heart failure; and (2) those due to emboli. In patients with subacute infection, the emboli are usually bland, causing infarction rather than infection. In individuals with acute bacterial endocarditis,

emboli are usually septic resulting in infarction, sup-pururation, or mycotic aneurysm. *Metastatic lesions* should be suspected when any patient with bacterial endocarditis develops an increase in temperature together with signs of a localized extracardiac process. Clearly, complications of therapy, such as phlebitis or drug allergy, as well as resistance of the infecting organism must first be ruled out. *Embolic lesions* can occur in virtually any organ. They are particularly common in the brain, myocardium, kidneys, liver, spleen and musculoskeletal system. They may occur in the lungs in patients with right-sided endocarditis. Careful physical examination, chest x-rays, electrocardiogram and urinalysis should be followed by radionuclide scans, ultrasound studies, CT scans or angiography, depending upon the type of lesion being sought. Anticoagulation is generally not recommended for these embolic events because of the risk of hemorrhage; however, patients with prosthetic valves should be maintained on their usual anticoagulant regimens.⁷ Suppurative emboli may result in multiple small abscesses (e.g. < 1 cm diameter) which generally respond to continued antibiotic therapy, or in larger abscesses (e.g. > 2 cm diameter) which require surgical drainage.

Cardiac and neurological complications are of crucial importance. The manifestations and treatment of the most common of these are outlined in Table 2. About one-third of patients with bacterial endocarditis develop *neurological complications*, with a mortality rate of almost 50%. *Cerebral embolism*, the most common of these, typically occurs in the first two weeks of acute endocarditis or later in the course of subacute endocarditis. The infarct usually involves the territory of the middle cerebral artery, producing hemiplegia and sensory deficit. Therapy is not well established; however, anticoagulation is generally contraindicated.⁷ If emboli are recurrent, and large vegetations are evident on echocardiography, valve surgery should be strongly considered. Neurosurgical operations are indicated for leaking or enlarging mycotic aneurysms and macroscopic brain abscess (Table 2).

There are several *indications for cardiac surgery* in bacterial endocarditis. One, mentioned above, is *recurrent embolization* to a crucial site, such as the central nervous system, in patients with large vegetations. Another is the development of *acute valvular insufficiency*, especially if associated with incipient heart failure and occurring despite optimal antimicrobial therapy.⁸ *Sinus of Valsalva aneurysm* usually necessitates surgery. *Septal myocardial abscess* is suggested by *electrocardiographic findings* of sudden prolongation of the PR interval or bundle branch block. If such an abscess is diagnosed, surgery may be lifesaving.⁹ *Suppurative pericarditis*, an unusual complication of acute bacterial endocarditis, is discussed later in this chapter. Finally, some patients exhibit continuously positive blood cultures despite optimal antibiotic therapy and without any clearcut metastatic foci to which the *refractory*

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Use in Lower Respiratory Disease. Antihistamines should NOT be used to treat lower respiratory tract symptoms including asthma

Antihistamines are also contraindicated in the following conditions: hypersensitivity to azatadine maleate and other antihistamines of similar chemical structure; monoamine oxidase inhibitor therapy (See **DRUG INTERACTIONS** Section).

WARNINGS Antihistamines should be used with considerable caution in patients with: narrow angle glaucoma; stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy, bladder neck obstruction

Use in Children: In infants and children especially, antihistamines in overdosage may cause hallucinations, convulsions, or death

As in adults, antihistamines may diminish mental alertness in children. In the young child, particularly, they may produce excitation.

OPTIMINE TABLETS ARE NOT INTENDED FOR USE IN CHILDREN UNDER 12 YEARS OF AGE

Use in Pregnancy Experience with this drug in pregnant women is inadequate to determine whether there exists a potential for harm to the developing fetus.

Use with CNS Depressants. Azatadine maleate has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc.)

Use in Activities Requiring Mental Alertness: Patients should be warned about engaging in activities requiring mental alertness, such as driving a car or operating appliances, machinery, etc

Use in the Elderly (approximately 60 years or older): Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients

PRECAUTIONS Azatadine maleate has an atropine-like action and, therefore, should be used with caution in patients with: a history of bronchial asthma, increased intraocular pressure, hyperthyroidism; cardiovascular disease, hypertension.

DRUG INTERACTIONS MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines.

ADVERSE REACTIONS The most frequent adverse reactions are underlined

General: Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose, and throat.

Cardiovascular System: Hypotension, headache, palpitations, tachycardia, extrasystoles

Hematologic System: Hemolytic anemia, thrombocytopenia, agranulocytosis

Nervous System: Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesias, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions.

Gastrointestinal System: Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.

Genitourinary System: Urinary frequency, difficult urination, urinary retention, early menses

Respiratory System: Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

OVERDOSAGE Antihistamine overdosage reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms (dry mouth, fixed, dilated pupils, flushing, and gastrointestinal symptoms) may also occur.

If vomiting has not occurred spontaneously, the patient should be induced to vomit. This is best done by having him drink a glass of water or milk after which he should be made to gag. Precautions against aspiration must be taken, especially in infants and children.

If vomiting is unsuccessful, gastric lavage is indicated within three hours after ingestion and even later if large amounts of milk or cream were given beforehand. Isotonic and ½ isotonic saline is the lavage solution of choice.

Saline cathartics, such as milk of magnesia, draw water into the bowel by osmosis and therefore are valuable for their action in rapid dilution of bowel content.

Stimulants should not be used

Vasopressors may be used to treat hypotension.

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TABLE 1

INITIAL THERAPY OF PRESUMED BACTEREMIA OF UNDETERMINED ETIOLOGY		
Probable portal of entry	Usual bacteriology	Suggested regimen*
Skin (e.g. suppurative phlebitis)	<i>Staphylococcus aureus</i>	Oxacillin, nafcillin or cephalosporin
	GNB**	+ Aminoglycoside*** or, possibly, cephalosporin alone
Pulmonary	<i>Streptococcus pneumoniae</i> <i>Staphylococcus aureus</i>	Oxacillin, nafcillin or cephalosporin
	GNB	+ Aminoglycoside
Urinary tract	Enterococcus	Ampicillin
	GNB	+ Aminoglycoside
Biliary tract	Enterococcus Clostridia	Ampicillin
	GNB	+ Aminoglycoside
GI tract and female genital tract	Anaerobes, including <i>Bacteroides fragilis</i>	Clindamycin, cefoxitin, carbenicillin, or chloramphenicol
	GNB	+ Aminoglycoside (might be omitted if cefoxitin is used)
Acute bacterial endocarditis	<i>Staphylococcus aureus</i> Streptococci Enterococcus	Nafcillin
	GNB, esp. <i>Pseudomonas aeruginosa</i>	+ Aminoglycoside
Subacute bacterial endocarditis	<i>Streptococcus viridans</i> Enterococcus	Penicillin G or ampicillin
		+ Streptomycin or gentamicin, for synergy against enterococcus
Typhoid fever	Salmonella	Ampicillin or chloramphenicol
No evident portal, esp. in immunosuppressed patients	Various	Carbenicillin or ticarcillin Cephalosporin Aminoglycoside

*These regimens should be modified when the infecting organism is identified and in patients with known or suspected allergies to the indicated drugs.

Typical intravenous dosages for adults with normal renal function are:

Oxacillin, nafcillin, 12 grams daily
Cefazolin, 6 grams daily; cephalothin, cefamandole, 8-12 grams daily
Gentamicin or tobramycin, 5 mg/kg/day; amikacin, 15 mg/kg/day
Ampicillin, 12 grams daily
Carbenicillin, 24-30 grams daily; ticarcillin, 16-20 grams daily
Clindamycin, 600 mg every 6 hours
Cefoxitin, 6-12 grams daily
Chloramphenicol, 4 grams daily
Penicillin G, 12-24 million units daily
Streptomycin, 500 mg intramuscularly twice daily

**GNB = gram-negative bacilli; primarily *Escherichia coli*, *Klebsiella sp.*, *Enterobacter sp.*, *Proteus sp.*, and *Pseudomonas aeruginosa*.

***Aminoglycoside here refers to gentamicin, tobramycin, or amikacin.

bacteremia can be attributed. In these individuals, valvular replacement may be the only way to control the disease. Surprisingly, the prosthetic valve rarely becomes infected during surgery in this circumstance.

When Does Bacteremia Signify Endocarditis?

Bacteremia may arise in a variety of settings, and

often can be cured by shorter courses of therapy than those required for endocarditis. Aside from stigmata such as "splinter" haemorrhages, glomerulitis, and positive rheumatoid factor, which point to subacute bacterial endocarditis, the following characteristics suggest that cardiac valvular infection is present: (a) continuous bacteremia, that is, the majority of

TABLE 2

NEUROLOGICAL AND CARDIAC COMPLICATIONS OF ACUTE BACTERIAL ENDOCARDITIS

Complication	Manifestations	Therapy
<i>Central nervous system</i>		
Cerebral embolism	Acute focal neurological change, abnormal CSF, lesion on EEG, brain scan or CT scan	Anticoagulation generally contraindicated. Consider valvular surgery for recurrent emboli with large vegetations detected on echocardiogram.
Cerebral mycotic aneurysm	Similar to above; arteriogram is usually diagnostic	Surgery indicated primarily for expanding or leaking lesions
Brain abscess	Similar to above; CT scan is extremely valuable in delineate lesions	Microscopic lesions can be treated with antibiotics alone; larger abscesses usually require surgery
<i>Cardiac</i>		
Heart failure due to valvular dysfunction	Physical signs of acute valvular insufficiency; echocardiogram may show premature mitral closure, flail valves; cardiac catheterization usually diagnostic	Valve replacement
Aneurysm of sinus of Valsalva	Continuous or biphasic murmur; coronary angiogram is usually diagnostic	Surgical repair
Septal myocardial abscess	Sudden bundle branch block or prolongation of PR interval	Not established; however, surgery seems the only modality likely to succeed
Suppurative pericarditis	Chest pain, widespread ST segment elevations on electrocardiogram; pericardial fluid on ultrasound	Pericardiocentesis, pericardial window or pericardiectomy

cultures positive over a period of hours or days; (b) gram-positive coccal bacteremia, i.e., staphylococcal, streptococcal or enterococcal; (c) cardiac murmur; and (d) no other evident source of bacteremia. In contrast, the finding of a discontinuous bacteremia and identification of a potential noncardiac source of the organisms suggest an extracardiac focus. It must be remembered that intravascular lesions such as suppurative phlebitis and infected vascular grafts also produce continuous bacteremias. If a noncardiac source of bacteremia can be identified and specifically treated or eliminated, a shorter course of treatment can be given depending on the nature of the local infection. However, the patient should be followed carefully for signs of incompletely treated endocarditis, namely, recurrent fever and changing murmur. If the factors cited above point to endocarditis, it is advisable to administer prolonged therapy, usually 4 weeks for subacute endocarditis and 4-6 weeks for acute disease.

RASH WITH FEVER

A wide variety of disorders can produce the sudden onset of rash with fever. The major diagnostic imperatives are outlined in Table 3. Bacterial endocarditis and other forms of *bacteremia* have been discussed earlier. Of these, staphylococcal, pneumococcal and streptococcal infection are the most likely to occur in a previously healthy adult. The rash may be of various kinds, but often produces local suppuration or necrosis. Disseminated intravascular coagulation may supervene. Initial therapy should in-

clude an anti-staphylococcal agent such as oxacillin, nafcillin, or a cephalosporin. In immunosuppressed patients, *gram-negative bacteremias* and *fungemia* may occur spontaneously. Diverse skin lesions may appear, often papular or necrotic. As with most of the entities discussed in this section, *aspiration or biopsy of the cutaneous lesions will often provide an excellent clue to the infecting organism*. Initial therapy in these patients should generally include an aminoglycoside antibiotic (Table 1).

About three-quarters of patients with *meningococcemia* have skin lesions. Large purpura signal the most fulminant disease with a fatality rate which exceeds 50%. Although definitive diagnosis is made by blood culture, a presumptive one may be reached by finding *gram-negative diplococci* in the aspirate of a *skin lesion* or in the *spinal fluid*. Penicillin G (24 million units per day) or ampicillin (12 grams per day) should be started as soon as blood cultures have been obtained if this diagnosis is seriously entertained.

Gonococcemia ("dermatitis-arthritis syndrome") is rarely fatal, but morbidity may be substantial if therapy is delayed. As the disease progresses, the tenosynovitis and diffuse arthralgia/arthritis may decrease and the infection may localize in one or more large joints. Blood cultures should be made, and aspirates of skin lesions or joint fluid should be examined for gram-positive diplococci. These aspirates, as well as swabs of the cervix and anus should be cultured on Thayer-Martin medium. A convenient oral regimen for disseminated gonococcal infection is

TABLE 3

DIAGNOSTIC IMPERATIVES IN PATIENTS WITH ACUTE ONSET OF RASH AND FEVER

Disease	Manifestations	Specific diagnosis	Suggested initial therapy*
Acute bacterial endocarditis	Fever, murmur (initially absent in one-third of patients), embolic skin lesions	Blood culture	Nafcillin (12 grams daily) + aminoglycoside
Other bacteremias (e.g. staphylococcal, streptococcal, <i>Pseudomonas aeruginosa</i> , <i>salmonella</i>)	Various rashes including symmetrical gangrene, necrotic skin lesions; typhoid produces "rose spots"	Blood culture	Various regimens according to clinical circumstances and gram-stained smears of skin aspirates (see Table 1)
Meningococemia	Often follows upper respiratory prodrome; fever, hypotension, macular or petechial skin lesions on distal extremities and trunk	Blood culture	Penicillin G (24 million units daily) or ampicillin (12 grams daily)
Gonococemia	Acute or subacute onset of fever, arthralgias, tenosynovitis; rash is pustular and/or petechial, favors extremities; often begins near time of menses in women	Culture of blood, joint fluid	Penicillin G 10 million units daily for 3 days or until clinical improvement, then oral ampicillin
Rocky Mountain spotted fever	Late spring and early summer in endemic areas; only 60% recall tick bite; headache, fever, rigors; rash appears about day 4, starts peripherally, maculopapules progress to petechiae; thrombocytopenia	Weil-Felix titer rise is presumptive evidence; specific complement fixation test is diagnostic	Tetracycline 2 grams daily; chloramphenicol is less desirable
Secondary syphilis	Any rash except vesicular or bullous; may be history or evidence of primary chancre	Serological test for syphilis; darkfield examination of lesions	2.4 million units of benzathine penicillin G (other regimens also available)

*Other regimens may be effective. Doses are for adults with normal renal function.

ampicillin 3.5 grams (or amoxicillin 3 grams) with probenecid 1 gram initially, followed by 500 mg of either antibiotic four times daily for seven days.¹⁰

Rocky Mountain spotted fever is suggested by the geographic setting, spring or summer season, and the rash, which usually appears about the fourth day of illness. Only sixty percent of patients remember a tick-bite.⁷ Hypotension, somnolence and confusion may be prominent. Thrombocytopenia is common. The fatality rate is about 20% in untreated patients and 5% in treated individuals. Tetracycline therapy should be started as soon as the disease is suspected, pending results of the Weil-Felix test. A definitive diagnosis can be made by demonstrating a rise in serologic titer to the specific rickettsial species.

Secondary syphilis is of importance both because it is contagious and because, if untreated, it can eventually progress to tertiary disease. The rash can be of any kind, except vesicular or bullous. It often shows discrete pink, maculopapules over the palms, soles and trunk. The serologic test for syphilis is almost always positive. The treatment is penicillin or tetracycline.

DISSEMINATED FUNGAL INFECTION

Disseminated fungal infection can occur in previously healthy individuals who live in, or visit, areas endemic for coccidioidomycosis (southwestern states) or histoplasmosis (midwestern states). The manifestations include fever, malaise, and diffuse involvement of major organs such as liver, lung, marrow and central nervous system. Disseminated coc-

cioidomycosis can be diagnosed serologically. The diagnosis of histoplasmosis must generally be made by biopsy. The treatment is amphotericin B.

Patients with immunosuppressive illnesses are susceptible to cryptococcal meningitis, disseminated candidiasis, aspergillosis, and mucormycosis. Unfortunately, blood cultures are rarely positive except in candidiasis. If skin lesions are present, these may be biopsied and examined by means of fungal stains. Likewise, lung, liver or bone marrow may be biopsied for histological examination and culture. Cryptococcal meningitis may be demonstrated by India ink preparation, culture, or demonstration of the antigen. The treatment of these infections is primarily amphotericin B. The concomitant administration of 5-fluorocytosine is warranted for cryptococcal meningitis.

PERICARDITIS AND MEDIASTITIS

Suppurative pericarditis is an uncommon disease which causes fever, chest pain, a pericardial friction rub and widespread ST-segment elevations on electrocardiogram. It is generally a complication of pneumonia or bacteremia, but occasionally follows trauma or is a complication of bacterial endocarditis. The usual etiologies are the pneumococcus, *Staphylococcus aureus* or *Haemophilus influenzae*. Treatment is surgical drainage together with antibiotic therapy based upon the results of gram-stain and culture of pericardial fluid.

Tuberculosis pericarditis typically presents with chronic systemic symptoms, including low-grade

fever and weight loss, and a large pericardial effusion. Pain is slight or lacking. Examination of pericardial fluid is rarely helpful. Pericardial biopsy is the usual mode of definitive diagnosis. Anti-tuberculous therapy with two drugs, including isoniazid, rifampin or ethambutol, is usually curative, and may be justified even without firm proof of the diagnosis if the clinical circumstances are sufficiently suggestive.

Suppurative mediastinitis is a rare but potentially fatal infection which may be a consequence of esophageal rupture, for example, due to instrumentation or violent vomiting. It may also follow mediastinal trauma or result from the downward dissection of a neck space infection. There is generally severe toxicity and chest pain. A precordial "crunch" may be heard. There may be subcutaneous emphysema and superior vena caval obstruction. The usual treatment is urgent surgical drainage together with antibiotics. The choice of the latter depends upon the clinical setting and results of cultures, but may initially include a penicillin and aminoglycoside.

PNEUMONIA

The list of treatable causes of pneumonia is too lengthy to be discussed in the limited space available. In most instances, a definitive diagnosis of treatable disorders can be made by gram-stain and culture of sputum, pleural fluid, and transtracheal or bronchoscopic aspirates, together with blood cultures. In some cases, these tests are not revealing and the patient fails to respond to the antimicrobial agents administered.

Pleural empyema is a cause of persistent fever in patients with bacterial pneumonia. Although chest x-ray will usually suggest this complication, sub-pulmonic or other loculated collections may be overlooked, especially when contiguous to an area of dense pulmonic infiltration. Re-examination, perhaps with tomograms, ultrasound or CT scan, may provide a clue to an empyema. If there is a suggestion of empyema, a needle aspiration should be performed. The treatment is drainage together with antibiotics.

Legionnaire's disease is due to a bacterium of uncertain taxonomy. It is more common in older persons. The radiographic findings are variable and nonspecific. Clues to the diagnosis include confusion, diarrhea, and, sometimes, chest pain.¹¹ Liver function tests may be mildly abnormal and there may be hypophosphatemia. At present, the diagnosis is generally made retrospectively by immunological means. Thus, it is usually necessary to administer therapy presumptively. The treatment is oral or intravenous erythromycin.¹²

Tuberculosis should be kept in mind in persons with a high risk of exposure, including medical personnel, individuals from endemic areas, and alcoholics. The disease may spare the upper lobes entirely. Furthermore, the *tuberculin skin test* is negative in 10-20% of infected individuals and in a higher proportion of severely debilitated ones. The

TABLE 4

TREATABLE INFECTIVE PNEUMONIAS OCCURRING IN IMMUNOSUPPRESSED PATIENTS

Radiographic pattern	Organisms commonly responsible	Treatment*
Diffuse alveolar or alveolar-interstitial	<i>Pneumocystis carinii</i>	Co-trimoxazole 20/100 mg/kg/day
Nodular or cavitary disease or nonspecific pneumonia	Bacterial infection, e.g. <i>S. aureus</i> or gram-negative bacilli	Antibiotics, depending on results of culture
	<i>Nocardia</i>	Sulfonamides, e.g. sulfisoxazole 6-9 gm/day
	<i>Aspergillus</i> , mucormycosis, cryptococcus, candida	Amphotericin B 0.4 mg/kg/day

*Suggested regimens in adults with normal renal function. Standard textbooks should be consulted for details of therapy and toxicity.

diagnosis in cavitary lung disease can usually be made by smear and culture of sputum or gastric washings though bronchoscopy is sometimes necessary. In non-cavitary disease, the diagnosis may be more difficult. If suspicion is sufficiently aroused, treatment with two drugs, including isoniazid, ethambutol, or rifampin, should be given presumptively.

Psittacosis is rare in this country. However, the fatality rate may be as great as 20%. Accordingly, every patient with a non-responding pneumonia should be asked about *exposure to birds* (sick or healthy). The diagnosis is made serologically. Tetracycline therapy, administered presumptively is usually effective.

Pneumonias in Immunosuppressed Patients:

These entities pose special problems both because of the unusual nature of some of the pathogens encountered, and because aggressive diagnostic maneuvers must usually be taken to ascertain the diagnosis. A detailed discussion of this problem is beyond the scope of this chapter. However, some of the more important diagnostic imperatives are summarized in Table 4.

Many of the pneumonias occurring in immunosuppressed patients are of "ordinary" types, i.e., due to the pneumococcus, *H. influenzae*, and other usual pathogens. Moreover, non-infectious diseases such as intrapulmonary haemorrhage, spread of tumor within the lungs, or radiation pneumonitis can produce similar pulmonary reactions. Nonetheless, unusual infectious etiologies are responsible for the pneumonias in at least one-third of these individuals, especially those with advanced underlying diseases who are receiving potent immunosuppressive agents. Diagnosis cannot generally be made by examining sputum. More aggressive techniques including *transbronchoscopic or open lung biopsy* are fre-

TABLE 5

DIAGNOSTIC IMPERATIVES IN PATIENTS WITH DIARRHEA		
Disease	Manifestations and Diagnosis	Treatment
Giardiasis	Prolonged diarrhea, non-bloody, afebrile, \pm mild malabsorption; diagnosis by examination of stool, duodenal aspirate or biopsy	Metronidazole 250 mg tid for 10 days or Quinacrine 100 mg tid for 5 days
Intestinal amebiasis	Travel history or homosexual exposure; cramps, fever	Metronidazole 750 mg tid for 5-10 days Diiodohydroxyquin 650 mg tid for 3 weeks
<i>Yersinia enterocolitica</i>	Prolonged diarrhea, low-grade fever, cramps, possibly skin, joint, or ocular manifestations; culture, or more commonly, serological tests, establish the diagnosis	Not well-established; trimethoprim-sulfa, chloramphenicol or tetracycline for several weeks may be effective
Pseudomembranous colitis	Fever and colitis in relation to a course of antibiotic therapy; sigmoidoscopic appearance and stool toxin titer are diagnostic	Vancomycin 125-500 mg po qid

quently necessary. These approaches should be readily resorted to, under coverage of platelet transfusion if there is severe thrombocytopenia, as soon as it is clear that the patient is not improving on antibacterial therapy and no other diagnosis can be established. Although tuberculosis should also be considered, it is curiously rare in these individuals.

URINARY TRACT INFECTIONS

Cystitis and pyelonephritis usually are easily diagnosed. By contrast, *renal carbuncle* and *perinephric abscess* may present as elusive causes of fever. These infections generally arise in the course of bacteremia or as complications of pyelonephritis. They contain either staphylococci or gram-negative bacilli. Because perinephric abscesses do not communicate with the urine and renal carbuncles do so irregularly, the urinalysis may not be abnormal. Fever, costovertebral angle tenderness, and, on occasion, a positive "psoas" sign should suggest the necessity for intravenous pyelography. Inspiratory and expiratory tomograms will usually show an immobile kidney in patients with perinephric abscess. Antibiotics and, in the case of perinephric abscess, surgery, are effective therapy.

Prostatic abscess may be an occult cause of fever and bacteremia. Occasionally, osteomyelitis of the lumbosacral spine occurs as a metastatic complication. Prostatic abscess can usually be suspected from the physical examination.

Tuberculous genitourinary infection may involve the upper or lower genitourinary tract. It should be considered in patients with sterile pyuria, strictures of the renal calyces, ureter or bladder, or tender swellings in the prostate, epididymis, or vas deferens. The chest x-ray is often normal. Several morning urine specimens should be obtained for culture; these

are usually positive in active disease. Tuberculosis of the female genital tract may be the cause of infertility, fever, and pelvic pain. The diagnosis may be exceedingly difficult and it is often made incidentally at surgery for a different presumed disease. Biopsy of endometrium, Fallopian tube or other involved area is usually positive. The treatment of these diseases is primarily chemotherapeutic.

DIARRHEAL DISEASE

The majority of diarrheal disease which occurs in North America is transitory, self-limited, and more inconvenient than serious. However, several entities merit special attention (Table 5).

Giardiasis is a moderately common cause of prolonged diarrhea in the United States. Parasites can be seen in the stool of about half of patients with this disease. If this examination is negative, duodenal aspiration or biopsy provide a more sensitive diagnostic test. The treatment is metronidazole or quinacrine.

The possibility of amebiasis as a cause of colitis should be suspected from the travel history. Homosexuals may contract this disease from their sexual activities. Careful microscopic examination of fresh stool and of material obtained from mucosal "crypts" at sigmoidoscopy will help to make the diagnosis. Serological tests may be useful in difficult cases and are recommended by some authorities as a routine screening procedure before patients with presumed "ulcerative colitis" are given steroids. The treatment is metronidazole or tetracycline.

Salmonellosis or shigellosis occasionally causes prolonged diarrhea and low grade fever. They are usually readily diagnosed by stool culture. Antibiotic therapy, for example, with oral ampicillin, is effective. *Yersinia enterocolitica* is becoming increasingly

TABLE 6

SELECTED DIAGNOSTIC IMPERATIVES IN PATIENTS WITH SUSPECTED INTRA-ABDOMINAL INFECTION

<i>Disease</i>	<i>Manifestations</i>	<i>Diagnosis</i>	<i>Treatment</i>
Liver abscess	Fever, elevated alkaline phosphatase, low serum albumin, and, possibly, enlarged, tender liver	Ultrasound, technetium or gallium scan of the liver	Macroscopic abscesses must be drained surgically; microscopic ones respond to antibiotics alone
Pancreatic abscess	Fever, leukocytosis, mid-abdominal tenderness and back pain in a patient with known pancreatic disease; palpable mass	Ultrasound and CT scan helpful. May be difficult to distinguish from pseudocyst except by extent of fever, leukocytosis	Antibiotics (broad spectrum) with surgical drainage
Subphrenic abscess	Unexplained fever following abdominal surgery of trauma; possible scapular pain, subcostal tenderness, sympathetic pleural effusion, elevated hemidiaphragm	Ultrasound, CT scan; barium studies of intestine; gallium scan	Surgical drainage; antibiotics
Retroperitoneal space infection	Fever, possibly flank pain or costovertebral angle tenderness, "psoas sign" in patient with renal, cecal, appendiceal, sigmoid, or duodenal focus of infection	Ultrasound; CT scan; IVP may show ureteral displacement	Surgical drainage; antibiotics
Pelvic thrombophlebitis	Usually in women with known pelvic infection, fever responds poorly to "appropriate" antibiotics; fleeting chest pains, dyspnea, hypoxemia	Diminished pO ₂ (< 80 mm Hg); lung scan; pulmonary arteriogram	Heparin
Tuberculous peritonitis	Unexplained fever, ascites, abdominal discomfort often without evident TB elsewhere	Usually requires peritoneal biopsy for histology and culture	Anti-tuberculous therapy, usually with three drugs

recognized as a cause of diarrhea, mild fever, and in some instances, joint pains and rash, particularly in the form of erythema nodosum. Conjunctivitis may also occur and the constellation may be reminiscent of the protean manifestations of inflammatory bowel disease. The diagnosis can sometimes be made by culture of the stool. The laboratory should be notified so that special techniques such as cold enrichment can be used. More often, the diagnosis is made by serological testing. The treatment is not well established. However, trimethoprim-sulfa or chloramphenicol would be suggested on the basis of *in vitro* susceptibility tests.

Inflammatory bowel disease is discussed elsewhere (see chapter on Gastrointestinal Diseases).

Pseudomembranous colitis has long been recognized as a complication of antibiotic therapy, especially with clindamycin. Diarrhea, fever, and sometimes colonic dilatation occur in close temporal relation to a course of antibiotics. Sigmoidoscopic examination shows characteristic pseudomembranes, and stool cultures may yield the toxigenic organism, *Clostridium difficile*. In some centers, a stool toxin assay is available for diagnosis. Various treatments are being studied. At present, vancomycin is probably the most commonly used form of therapy.

INTRA-ABDOMINAL INFECTIONS

Most intra-abdominal infections can be regarded as diagnostic imperatives. Many, such as acute ap-

pendicitis, colonic diverticulitis, and ascending cholangitis, are readily considered and promptly diagnosed once the possibility of intra-abdominal sepsis has been raised. A complete listing of these disorders is beyond the scope of this chapter. Therefore, I have selected a small number which are of special interest because they may be comparatively subtle but catastrophic. They are summarized in Table 6.

Liver abscess should be suspected in patients with fever, an elevated alkaline phosphatase, and a decreased serum albumin concentration. *Microscopic abscesses* may arise from biliary tract infection or bacteremia, and respond to antimicrobial therapy. Occasionally, intra-abdominal infection, for example, from a ruptured appendix or colonic diverticulum, may give rise to thrombosis and infection of the portal vein (pyelephlebitis); this, in turn, produces metastatic liver abscesses, fever, jaundice, and a large, tender, liver.

Macroscopic liver abscesses may be the consequence of biliary tract infection, direct spread from a perihepatic focus, or bacteremic seeding of a hepatic hematoma.¹³ Such hematomas are often secondary to blunt abdominal trauma. Large abscesses can be delineated by technetium liver-spleen scan, CT scan, or ultrasound. The treatment is surgical drainage together with antibiotic therapy based upon the results of culture. In patients with an appropriate residential history, amebic abscess or hydatid cyst of

the liver should be considered.

Pancreatic abscess should be suspected when fever, leukocytosis and abdominal or back pain develop in a patient with known pancreatic disease. A mass is palpable in about two-thirds of patients and is usually demonstrable behind the stomach on x-ray. The major condition to be differentiated from this is pancreatic pseudocyst.¹⁴ Fever and leukocytosis point to abscess rather than pseudocyst. The serum amylase is normal in about half of patients with either disease. Because pancreatic pseudocysts often resolve without surgery, they should simply be carefully observed. In contrast, pancreatic abscess is almost uniformly fatal without surgery; with surgical drainage, over 50% of patients survive.

Subphrenic abscess is a notoriously elusive infection which should be considered in any patient with unexplained fever following abdominal surgery or trauma. Only one-quarter of patients have paralysis of the hemidiaphragm on chest fluoroscopy. *Retroperitoneal space infections* can be equally elusive. Clues such as back pain and costovertebral angle tenderness are often lacking. If the clinical circumstances are appropriate, for example, in a patient with recent urinary tract infection, ruptured appendix or sigmoid diverticulum, or with a positive "psoas" or "obturator" sign on physical examination, noninvasive studies should be undertaken to examine the retroperitoneal space (Table 6).

Pelvic thrombophlebitis with septic pulmonary emboli is an outstanding example of a diagnostic imperative. This entity should be considered in any patient who, *following childbirth, pelvic surgery or pelvic sepsis, has spiking temperatures which are unresponsive to antibiotic therapy*. There are often symptoms pointing to pulmonary embolism, such as fleeting chest pains and episodes of dyspnea, but these may be lacking. An arterial blood gas and lung scan can be used to substantiate the diagnosis. The most direct approach is a therapeutic trial of heparin. This should not be delayed if there is a high index of suspicion. Dramatic defervescence should occur within 24-48 hours. If not, other diagnoses such as undrained pelvic abscess should be entertained.

Tuberculous peritonitis is usually of relatively sudden onset. Because it lacks distinctive features, this disorder is easily misdiagnosed. The possibility should be considered in all patients with fever, unexplained ascites, and more than a few hundred inflammatory cells per mm³ in the ascitic fluid. The peritoneal fluid usually exhibits a high protein content and a predominance of lymphocytes, though granulocytes may be prominent early in the disease. The organism can be cultured from the ascitic fluid in fewer than 20% of cases. Peritoneal biopsy for histologic examination and culture usually is diagnostic.

HEPATITIS

Most patients with "hepatitis" have viral infections. In rare instances, the symptoms may be due to

other diseases requiring specific therapy. These possibilities should be considered in patients in whom the clinical picture does not evolve in atypical fashion. As a rule, the hepatic enzyme elevations are not as great in these disorders as in garden-variety viral hepatitis.

Ascending cholangitis due to biliary tract disease may masquerade as hepatitis. There usually is a rise in alkaline phosphatase and bilirubin which is disproportionate to the SGOT, SGPT and LDH. In addition, there is a polymorphonuclear leukocytosis. Therapy should include antibiotics (Table 1) and consideration of surgery for the underlying disorder of the biliary tract. A similar picture can be seen in patients with *liver abscess*, discussed above. A third common disease which rarely can present as "hepatitis" is *subacute bacterial endocarditis*. Occasionally, the hepatic component dominates the clinical picture. The true cause is readily diagnosed by blood culture. Finally, there are exceptional cases in which *syphilis* causes a hepatitis, usually characterized by a relatively high alkaline phosphatase value.¹⁵ The diagnosis is established serologically.

BONE, JOINT AND SOFT-TISSUE INFECTIONS

Although most entities in this category are readily suspected and diagnosed, several commonly elude diagnosis until late in their course.

Tuberculous infection should be suspected in any patient with a chronic, focal, inflammatory lesion of bone, joint or soft-tissue. Fever and systemic signs may be minimal and the chest x-ray may be normal. Tuberculous osteomyelitis of the spine usually involves the lower thoracic or upper lumbar vertebrae. The x-ray shows narrowing of the intervertebral space and, possibly, a paravertebral abscess. The diagnosis is confirmed by needle aspirate or biopsy of the infected area. Treatment is primarily chemotherapeutic.

Spinal epidural abscess is a diagnostic imperative of the first order. It should be considered in any patient with *fever, back pain and nerve root pain*. By the time neurological signs are evident in the lower extremities, the process is far advanced. The infection often arises from a contiguous vertebral osteomyelitis which produces localized tenderness over the spine; however, this may not be evident radiographically at the time the patient presents. In one-quarter of cases, the epidural collection appears to arise from a bacteremia. In a smaller percentage, it is a postoperative complication. Depending on the source of infection, the abscess may contain *Staphylococcus aureus* or gram-negative bacilli. Although the prodrome of fever and back pain may be rather indolent, the disease often evolves explosively following the appearance of root pain. Spine films should be obtained and CSF puncture should be performed on an emergency basis. If lumbar involvement is suspected, the puncture may be done via the lateral cervical route. The CSF shows markedly increased protein and a mild pleiocytosis. Myelography should

TABLE 7

DIFFERENTIAL DIAGNOSIS OF SOME ANAEROBIC SOFT TISSUE INFECTIONS

Characteristic	<i>Clostridial</i> <i>Cellulitis</i>	<i>Clostridial</i> <i>Myonecrosis</i> (<i>Gas Gangrene</i>)	<i>Anaerobic</i> <i>Streptococcal</i> <i>Myonecrosis</i>	<i>Necrotizing</i> <i>Fasciitis</i>	<i>Synergistic</i> <i>Necrotizing</i> <i>Cellulitis</i>
Toxemia	±	+	+	+	+
Local pain	±	+	+	+	+
Local swelling	±	+	+	+	+
Gas	++ to ++++	++	++	±	±
Appearance of skin	Essentially normal	Tense, white, or gangrenous with bullae	May be coppery	Brawny; pale red or gangrenous	Swollen, red or gangrenous
Gross characteristics of exudate	Putrid, brown	Thin, serous; may be sweetish or putrid	Seropurulent, sour	Variable	Purulent, putrid
Gram stain of exudate	Abundant PMNs Gram-positive rods	Few PMNs Gram-positive rods	Many PMNs Gram-positive cocci	Many PMNs Variable, sometimes mixed organisms	Variable PMNs Mixed organisms
Etiology	Clostridia	Clostridia	Anaerobic streptococci; (± aerobic streptococci, staphylococci)	Aerobic and anaerobic streptococci and staphylococci; occasionally <i>Bacteroides</i>	Mixed—anaerobic streptococci, <i>Bacteroides</i> , and coliforms
Surgical therapy	Judicious incision and debridement	Extensive removal of all infected muscle	Remove necrotic muscle	Widespread filleting incisions if no response to antibiotics	Widespread filleting incisions

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be performed promptly followed by urgent surgical drainage of the epidural abscess. The epidural infection should be treated with systemic antibiotics for 3-4 weeks; concomitant vertebral osteomyelitis should be treated for at least 6 weeks.¹⁶

Suppurative arthritis is usually easily diagnosed. However, when a patient with known articular disease such as rheumatoid arthritis develops an inflamed joint, especially in the absence of a flareup of disease in other joints, suppurative arthritis should be considered. Joint fluid should be aspirated for microscopic examination and culture.

Anaerobic Soft-tissues Infections:

Among the most serious of *soft-tissue infections* are those due to anaerobic bacteria or mixtures of anaerobic and aerobic organisms. Some characteristics entities are outlined in Table 7. These lesions generally occur in areas of trauma and deficient vascular supply. The presence of infection is readily suspected, but not its extent or portent. *Aspiration and gram-stain of material from the lesion* is a crucial procedure which usually provides valuable information as to the species of infecting organism(s). If streptococci are seen, the antibiotic regimen should

include high doses of penicillin G (e.g. 20 million units per day) or ampicillin (e.g. 12 grams per day); the same applies to clostridia. In penicillin-allergic patients, a cephalosporin or clindamycin may be administered instead. However, a cephalosporin should not be given if the allergy was severe, for example, a giant urticaria or anaphylaxis. If thin, pleomorphic gram-negative rods are found, suggesting *Bacteroides fragilis*, clindamycin, cefoxitin, ticarcillin, carbenicillin, or possibly, chloramphenicol, should be included in the regimen. Gram-negative enteric bacilli should generally be treated with an aminoglycoside until their sensitivity has been established. *Widespread surgical debridement* is as important as antibiotic therapy for most of these lesions (Table 7) and must not be delayed.

It should be apparent from Table 7 that the finding of clostridia in a wound is not necessarily indicative of myonecrosis. Indeed, these organisms may colonize wounds without causing infection. *Clostridial myonecrosis*, or "gas gangrene" should be thought of when, following trauma or surgery, a quiescent interval is followed by local pain, swelling and crepitus together with signs of systemic toxicity. X-rays show gas in the tissues and the wound exudate contains

TABLE 8

SPINAL FLUID "PROFILES" IN MENINGITIS AND RELATED DISEASES

Disease	Purulent Profile	Clues to Diagnosis
<i>Common causes</i>		
Bacterial meningitis	Gram-stain and culture of CSF	
<i>Uncommon causes</i>		
Viral meningitis (early)	Profile becomes lymphocytic within 12-24 hrs.	
Cerebral embolus in bacterial endocarditis	Heart murmur; evidence of other emboli; blood cultures; CSF glucose usually normal	
Parameningeal infections (e.g. subdural empyema, leaking brain abscess)	Evidence of infection in sinuses, middle ear or other location; skull x-rays, EEG, brain scan or CT scan demonstrate lesion; CSF glucose usually normal	
Tuberculous (early)	Profile becomes lymphocytic within 2-3 days; may be ancillary evidence of TB; AFB smear occasionally positive	
Herpes simplex encephalitis	Striking cerebral localization (esp. to temporo-parietal lobes); rapid impairment of consciousness; CSF glucose usually not markedly depressed, and < 85-90% polymorphonuclear leukocytes; gram-stain and culture negative	
<i>Lymphocytic low-glucose profile</i>		
Disease		Clues to Diagnosis
<i>Common causes</i>		
Tuberculous meningitis	Suggested by ancillary evidence (e.g. history of exposure, abnormal chest x-ray, positive PPD—but these may be absent); AFB smear; failure of ordinary bacteria to grow or of patient to respond to antibiotic in compatible clinical setting (see text)	
Fungal meningitis	Detection of cryptococcal antigen in CSF (e.g. latex agglutination); endemic areas (coccidioidomycosis); immunosuppressed patient; development of meningitis during systemic fungal infection	
<i>Uncommon causes</i>		
Partially-treated bacterial meningitis	Recent administration of antibiotics; see text for management of this problem	
Spirochetal	Syphilis—positive serologic tests Leptospirosis—ancillary findings (conjunctivitis, hepatitis, nephritis, etc), serology	
Sarcoidosis	Ancillary findings (hilar adenopathy, eye involvement, hypergammaglobulinemia, cutaneous anergy)	
<i>Lymphocytic normal-glucose profile</i>		
Disease		Clues to Diagnosis
<i>Common causes</i>		
Viral meningitis or encephalitis	May occur in setting of an epidemic; course <i>usually</i> benign; CSF glucose remains essentially normal; cultures negative	
<i>Uncommon causes</i>		
Partially-treated bacterial meningitis	Recent administration of antibiotic; see text for management of this problem	
Parameningeal infection	See “Purulent profile” above	
Tuberculous or fungal meningitis (early)	Serial taps usually show decreasing CSF glucose; (see “Lymphocytic low-glucose profile”)	

gram-positive rods. Features permitting distinction from the much less serious condition of clostridial cellulitis are shown in the table. Radical surgery together with high-dose penicillin G constitute usual therapy of gas gangrene.

Tetanus:

Tetanus is rare in this country, but carries a fatality rate of about 50%. It should be suspected when muscle cramps or spasticity follow a wound in a patient who is incompletely immunized against the disease. Although trismus eventually appears in over half of patients, earlier manifestations may consist only of episodic spasms of the back or abdominal muscles.

The diagnosis is a clinical one. If there is reasonable suspicion, tetanus immune globulin should be given promptly.¹⁷ Surgical debridement and antibiotic therapy may be indicated, depending on the state of the wound.

MENINGITIS

Diagnosis:

Meningitis should be the first consideration in any patient with fever, headache and a stiff neck. Older, or markedly debilitated patients may have little or no nuchal rigidity. In these instances, the physician must be ready to perform a cerebrospinal fluid tap on minimal indications such as fever and unexplained

TABLE 9

INITIAL ANTIBIOTIC THERAPY FOR PRESUMED ACUTE BACTERIAL MENINGITIS OF UNCERTAIN ETIOLOGY IN ADULTS

<i>Usual etiologies</i>	<i>Suggested therapy (dosages apply to adults with normal renal function)</i>
<i>Acute sporadic meningitis</i>	
Pneumococcus (50%)	Penicillin G 2 million units every 2 hours or ampicillin 12 grams daily IV
Meningococcus (15%)	
<i>H. influenzae</i>	If staphylococci seen on gram stain, change to oxacillin or nafcillin 12 grams daily IV
Streptococci	
Staphylococci	
Listeria	
Gram-negative bacilli (<10%)	If gram-negative bacilli seen, chloramphenicol should be given, 4 grams daily IV, plus intrathecal gentamicin, 2-5 mg, pending identification and sensitivity tests
<i>Immunosuppressed host</i>	
<i>Staphylococcus aureus</i>	
Streptococci	Oxacillin or nafcillin (12 grams daily IV) plus intrathecal gentamicin (2-5 mg)
Gram-negative bacilli	
Listeria	Chloramphenicol (4 grams daily IV) or carbenicillin (30 grams daily IV) could be substituted for the penicillin provided intrathecal aminoglycoside is given
Non-bacterial (e.g. cryptococcus)	Depends on etiology
<i>Meningitis developing in hospital, or post-traumatic or post-neurosurgical</i>	
	Same as Immunosuppressed host
<i>Staphylococcus aureus</i>	
Streptococci (including enterococcus)	
Gram-negative bacilli	

*Dosages apply to adults with normal renal function. Chloramphenicol is generally a good substitute for penicillin G in penicillin-allergic patients. Many strains of *H. influenzae* are now ampicillin-resistant; chloramphenicol is usually effective. Cephalosporins, clindamycin and aminoglycosides do not penetrate the meninges well following systemic administration.

confusion. If acute meningitis is diagnosed, blood and CSF should be obtained for culture and antibiotics should be instituted within the hour. If there are signs of *elevated intracranial pressure*, for example, nausea, vomiting, or papilledema, *lumbar puncture may result in herniation*. In this situation, the procedure should not be done and neurosurgical opinion should be sought regarding the possibility of a ventricular puncture. The CT scan can be helpful in assessing the likelihood of raised intracranial pressure by demonstrating dilated ventricles, but resort to this useful test should not be permitted to result in a substantial delay in starting therapy. Analysis of the CSF is crucial for four reasons: (1) it permits establishment of a spinal fluid profile (Table 8); (2) organisms may be seen on gram-stain; (3) the fluid can be analyzed for lactate concentration (cf below); (4) the fluid can be cultured.

Treatment:

If gram-positive cocci are seen in the CSF, pneumococcal meningitis is likely and high-dose penicillin G or ampicillin should be administered (Table 9). If gram-negative diplococci are found, meningococcal infection is most likely. The treatment is the same as for pneumococcal infection. *Haemophilus influenzae* is suggested by the finding of small, pleomorphic gram-negative rods, and is the

most common cause of meningitis in children. Initial therapy should include chloramphenicol because of the possibility of ampicillin-resistant organisms. *H. influenzae* are sometimes mistaken for meningococci. If there is any doubt of the diagnosis, ampicillin, or possibly chloramphenicol, should be given rather than penicillin G.

In patients who are *immunosuppressed*, or who *develop meningitis while in the hospital or following trauma*, the possibility of infection due to *S. aureus* or gram-negative enteric bacilli looms large.¹⁸ Intrathecal aminoglycoside, for example, gentamicin, should generally be administered, together with oxacillin, nafcillin, chloramphenicol or carbenicillin for activity against staphylococci, streptococci and listeria. (Although carbenicillin is not active against staphylococci, aminoglycoside will usually provide adequate temporary coverage pending culture results.) It must be emphasized that aminoglycosides, clindamycin, and cephalosporins penetrate the central nervous system very poorly after systemic administration and are not dependable by this route for treatment of meningitis.

Differential Diagnosis:

A number of conditions, many of them diagnostic imperatives, may cause fever and headache and yield

an abnormal CSF. A helpful approach to the interpretation of the spinal fluid findings has been provided by Hyslop and Swartz.¹⁹ Table 8 is based on their analysis. The "purulent profile" shows a predominance of polymorphonuclear leukocytes, a low glucose concentration, an elevated protein. The "lymphocytic low-glucose profile and "lymphocytic normal-glucose" profile are self-explanatory. There may be variable elevations in protein concentration in these different entities.

Several points are worthy of special note.

Patients who develop *recurrent meningitis*, usually pneumococcal, should be examined for sickle-cell disease, hypogammaglobulinemia, asplenia, or dural leak. Careful inquiry should be made about remote head trauma. In the absence of another cause, a dural communication should be presumed and carefully sought by radiographic studies.

Cerebellar abscess is among the most difficult of parameningeal foci to identify. It should be suspected in patients with fever, headache, increased intracranial pressure, cerebellar signs which may be quite subtle, and a lymphocytic normal-glucose profile. Lumbar puncture should be done cautiously in such patients and neurosurgical consultation may be advisable before the procedure is attempted. A ventricular tap may be necessary in this instance.

Partially-treated bacterial meningitis may be difficult to distinguish from viral, tuberculous or fungal infection. If the patient appears quite ill, penicillin G, ampicillin, or chloramphenicol therapy should be administered while the workup progresses. Otherwise antibiotics may be withheld and the patient carefully observed. A repeat tap in eight or twelve hours generally will show evolution toward a purulent profile in bacterial infection and toward a lymphocytic-normal glucose profile in viral disease. Tuberculous or fungal processes usually maintain a lymphocytic low-glucose pattern. A helpful clue is to measure the *spinal fluid lactate concentration* which is usually below 35 mg/100 ml in viral meningitis.²⁰

ENCEPHALITIS

Both encephalitis and meningitis often cause fever, confusion and somnolence. However, headache and nuchal rigidity are more prominent in meningitis while signs of deep cerebral involvement such as stupor, aphasia, hemiplegia, or convulsions are characteristic of encephalitis. The CSF is usually more strikingly abnormal in meningitis than in encephalitis; it is essentially normal in encephalopathy. Clearly, however, encephalitis and meningitis may overlap. Indeed, they may coexist in various viral infections.

Several important treatable infectious diseases may resemble encephalitis or encephalopathy, including *brain abscess*, *bacterial endocarditis* with cerebral emboli, *typhoid fever*, *Rocky Mountain spotted fever*, and *Legionnaire's disease*, all of which are described elsewhere in this chapter. Cerebral malaria due to *M. falciparum* should be considered in

travellers returning from endemic areas: the diagnosis is made by examination of blood smears. *Mycoplasma pneumoniae* infections occasionally cause psychosis, encephalitis, cerebellar dysfunction, meningitis, or transverse myelitis.²¹ This diagnosis should be considered in patients with the acute onset of unexplained central nervous system disease and pulmonary infiltrates. It is supported by finding an elevated titer of cold agglutinins. Although there is no firm evidence that erythromycin or tetracycline is effective for this complication, one of these agents should probably be administered if the picture is sufficiently suggestive.

Herpes simplex encephalitis is the most common cause of fatal sporadic encephalitis in this country and is the only treatable viral encephalitis. The onset may be abrupt. In addition to signs of encephalitis, there are usually features of temporo-parietal localization such as aphasia, focal seizures and weakness on physical examination. This is supported by localized abnormalities on EEG, CT scan, radio-nuclide brain scan, or arteriography. The CSF may show polymorphonuclear leukocytosis, erythrocytes and a low glucose which bespeak the necrotizing nature of this viral infection. Diagnosis is established by biopsy and culture of the clinically-involved area of the brain. The treatment is intravenous vidarabine.²²

FEVER OF UNKNOWN ORIGIN (FUO)

To qualify for the designation FUO, fever should exceed 100.5°F, be present for at least three weeks, and defy at least one week of investigation in hospital. Routine tests such as blood counts, urinalysis, chest x-ray, liver function tests, BUN and serum creatinine, should be performed and tuberculin skin test reactivity should be assessed using Candida antigen or streptokinase/streptodornase (SK/SD) as controls.

Intravenous pyelogram will help to rule out a hypernephroma, renal or perirenal abscess. Barium enema may disclose occult diverticulitis or tumor. Upper intestinal x-rays with a small bowel follow-through may permit a diagnosis of tumor or regional ileitis to be made.

Abnormalities of liver function tests, especially alkaline phosphatase, should suggest the possibility of ascending cholangitis, liver abscess, disseminated tuberculous or fungal infection, tumor, or chronic granulomatous hepatitis. Oral cholecystogram and radionuclide liver scan, may be helpful in elucidating the diagnosis and liver biopsy should be strongly considered. Abnormalities of the peripheral blood smear may indicate the need for examination of bone marrow. In endemic areas, disseminated histoplasmosis or coccidioidomycosis may be considered and appropriate serological tests should be performed.

For a fuller discussion of the problem of FUO, the reader is referred elsewhere.²³ I shall consider here only a few diagnostic imperatives that may defy the usual tests.

Tumors:

Atrial myxoma may be mistaken for culture-negative bacterial endocarditis. The diagnosis can usually be made with cardiac ultrasound.

Hodgkin's disease should be considered especially in individuals with prolonged fevers which wax and wane. If superficial nodes are not enlarged, deeper ones may be sought by mediastinal x-rays, gallium scan and lymphangiogram.

Hypernephroma may produce back pain and is often accompanied by microscopic hematuria. For reasons that are not clear, liver function tests may be abnormal even without liver metastases.

Multiple myeloma occasionally escapes detection as a cause of fever for many months. Bone pain may be complained of, the blood sedimentation rate is usually very high and anemia is generally present. Serum and urine electrophoresis should be repeated at intervals. Bone x-rays and possibly bone marrow biopsy may be helpful in suggesting the diagnosis.

Inflammatory conditions:

Inflammatory bowel disease may be easily missed if careful attention is not paid to the terminal ileum on x-ray. Some patients with this disease have minimal diarrhea and abdominal pain.

Polymyalgia rheumatica and *temporal arteritis* are common causes of FUO in elderly persons.²⁴ These patients often look surprisingly well considering the duration of symptoms. The erythrocyte sedimentation rate is usually very high and there may be mild abnormalities of liver function tests. Temporal artery biopsy is, unfortunately, often negative. If the clinical picture is sufficiently suggestive (see chapter on Rheumatology), a therapeutic trial of steroids is warranted. This approach should not be used if bacterial endocarditis and miliary tuberculous have not been firmly excluded.

Collagen-vascular diseases may present as occult fevers. Although the diagnosis is eventually suggested by the development of arthralgias, skin lesions, renal, or other abnormalities, the true nature of the underlying illness may escape detection for long periods. If serological studies (antinuclear antibody titer, rheumatoid factor, complement levels) are unavailing, the diagnosis will usually have to be made by biopsy of an involved organ.

Dissecting aneurysm of the aorta is a rare cause of FUO.

Familial Mediterranean Fever may be suspected in individuals of appropriate ancestry who have had unexplained, usually recurring attacks of fever, abdominal or joint pains. They often have relatives with a history of such episodes or of renal amyloidosis. Attacks can be prevented by prophylactic administration of colchicine.

Subacute thyroiditis is a rare cause of FUO. The diagnosis is easily missed if the patient dismisses the complaint of "sore throat" because of the normal pharynx and negative throat culture. Closer questioning and careful palpation of the thyroid should

point to the true focus of inflammation. Thyroid function tests including T4I, anti-thyroglobulin and antimicrosomal antibodies may be helpful in making the diagnosis. The disease responds to thyroid hormone although a short course of steroids is sometimes needed.

Infections:

Subacute bacterial endocarditis and disseminated tuberculosis are the most common infectious causes of FUO. If there is sufficient evidence of *endocarditis*, such as cardiac murmur, anemia, and unexplained azotemia, and the patient's condition is deteriorating, therapy may be warranted even without positive blood cultures. Penicillin G or ampicillin together with an aminoglycoside such as streptomycin constitute a fair therapeutic trial for the usual organisms. If there is no defervescence after a week or so of therapy, the diagnosis must be cast into serious doubt.

Miliary tuberculosis should be strongly considered in individuals with a high risk of exposure, such as medical personnel and persons from lower socioeconomic strata. There are usually abnormalities of the chest x-ray, liver function tests or marrow. If such features are present and the patient's condition is worsening, a trial of therapy with two drugs such as isoniazid and ethambutol is warranted, even without proof, while the diagnostic search continues. A response to therapy should be clearly evident within one or two weeks.

Disseminated fungal infection has been discussed earlier in this chapter.

On rare occasions, occult dental infection can present as FUO. Careful physical examination together with dental x-rays will usually lead to this diagnosis.

Among the most elusive and frustrating causes of FUO are *factitious* (simulated) and *self-induced fever*. The former is usually produced by manipulation or substitution of the thermometer, the latter by self-administration of infected or pyrogenic material. The patients are frequently young women who have some acquaintance with the health professions. Factitious fever should be suspected when there is little accompanying elevation in pulse, sedimentation rate, or other abnormal signs. Self-induced disease should be suspected when infections, usually bacterial, are inexplicably recurrent or persistent. A search of the patient's belongings may provide circumstantial evidence in the form of thermometers, syringes and needles. Confrontation is rarely helpful; indeed, it usually provokes the patient to run away. Because the patient will rarely consent to psychiatric interview, the physician is generally best advised to adopt a supportive, non-condemnatory posture. Advice may be sought from a psychiatrist regarding the likelihood of suicide in a particular patient. The passivity required of the physician caring for such patients is, in more than one respect, a form of testimony to the injunction "primum non nocere."

CONCLUDING COMMENT

Infectious diseases are among the most treatable of illnesses. However, the temptation to administer potent antibiotics must not be permitted to relegate to a shadowy corner the simple procedures of careful history-taking, physical examination, as well as aspiration and gram-stain of infected material. Failure of the disease to respond to antibacterial therapy should not dictate a blind leap to more toxic drugs, but should raise the possibility that other forms of therapy such as surgical drainage, corticosteroids, or heparin, may be necessary.

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Annual Meeting Dates For Your 1980 Calendar...

Maine Medical Association, June 12-15

The Balsams, Dixville Notch, New Hampshire

American Medical Association, July 20-24

Downtown Chicago Marriott, Chicago



CONTINUING MEDICAL EDUCATION IN MAINE

Conferences and Workshops

Title: Seminar on Sports Medicine
Date: June 30-July 3, 1980
Location: Bowdoin College, Brunswick
Sponsors: Regional Memorial Hospital and Bowdoin College
Credit: AMA and LCCME Category I—20 hours
Reg. Fee: Tuition \$240
For further information contact Office of Continuing Medical Education, Regional Memorial Hospital; 729-0181 Ext. 206.

Title: Family Medicine Update
Date: September 7-10, 1980
Location: Spruce Point Inn, Boothbay Harbor
Sponsors: AAFP and Medical Care Development
Credit: AMA and LCCME Category I—15 hours and AAFP (prescribed)—14 hours
Reg. Fee: \$150; \$120 for State of Maine AAFP members
For further information contact Gerald Goold, Medical Care Development; 622-7566.

Title: Third Annual Infectious Diseases Symposium
Date: September 27, 1980
Location: Schaeffer Theater, Bates College
Sponsors: St. Mary's General Hospital, Central Maine Medical Center, and Bates College
Credit: AMA and LCCME Category I—6 hours and AAFP (elective) 6 hours
Reg. Fee: \$10.00

Title: Tri-State Surgical Association Annual Meeting
Date: November 6-9, 1980
Location: Castle Harbor Hotel, Bermuda
Sponsor: Maine Chapter, American College of Surgeons
Credit: AMA and LCCME Category I—18 hours
Reg. Fee: To be determined
For further information contact John Towne, M.D.; 872-7713.

Programs Sponsored By Mid-Maine Medical Center/Colby College

Title: Obstetrics and Gynecology
Date: July 7-11, 1980
Credit: AMA and LCCME Category I; AAFP—18 hours
Title: Pediatrics
Date: July 14-18, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—16 hours

Title: Surgical Techniques
Date: July 15-18, 1980
Credit: AMA and LCCME Category I—16 hours
Title: Dermatology for the Non-Dermatologist
Date: July 24-28, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—16 hours

Title: Neurosurgical Techniques

Date: July 27-30, 1980
Credit: AMA and LCCME Category I—21 hours
Title: Otolaryngology
Date: August 3-7, 1980
Credit: AMA and LCCME Category I—18 hours
Title: Epilepsy
Date: August 5-8, 1980
Credit: AMA and LCCME Category I; AAFP—18 hours
Title: Ophthalmology
Date: August 10-14, 1980
Credit: AMA and LCCME Category I—18 hours
Title: Nuclear Medicine
Date: August 17-21, 1980
Credit: AMA and LCCME Category I—28 hours
Title: Medical and Surgical Emergencies
Date: August 19-22, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—25 hours

Title: Forensic Science
Date: August 24-27, 1980
Sponsors: In cooperation with the National Association of Medical Examiners
Credit: AMA and LCCME Category I; AAFP—24 hours
Title: Pulmonary Disease
Date: August 24-28, 1980
Credit: AMA and LCCME Category I—21 hours

All of the Colby activities will be based at the Colby College campus in Waterville. Registration fee is to be determined. For further information contact Robert Kany, Ph.D., Colby College; 873-1131 Ext. 267/251.

Hospital Activities

Augusta General Hospital Augusta, Maine

July 22, 1980 7:30-8:30 a.m. **Hypothermia**
Murray Hamlet, M.D., Army Institute of Environmental Medicine, Natick, Massachusetts

July 29, 1980 7:30-8:30 a.m. **Tumor Conference**
Speaker and topic to be announced
These programs have been certified AMA and LCCME Category I and AAFP (prescribed). ITS presentation. For further information contact Mrs. Nancy Favorite; 623-4711.

Central Maine Medical Center Lewiston, Maine

July 16, 1980 12 Noon **Ultrasonography in OB/GYN**
Miguelito Cabelin, M.D., Central Maine Medical Center

Every Thursday **Tumor Board** 12-1 p.m.
Every Friday **Medical Grand Rounds** 9-10 a.m.

4th Friday (Odd Months)	Joint Surgical Grand Rounds	7:45-8:45 a.m.
2nd Fridays	Visiting Professorship, Boston University	1-3 p.m.

All activities have been certified AMA and LCCME Category I. For further information contact Carol Murrell, Central Maine Medical Center; 795-2435.

Eastern Maine Medical Center Bangor, Maine

Every Mon.	EEG Conference	12-1 p.m.
Every Mon.	Surgical Service—Chief's Rounds	5-6 p.m.
4th Mon.	ENT Section Meeting	12-1 p.m.
4th Mon.	Neurosurgery Section Meetings	4-5 p.m.
3rd Tues.	Dermatology-Pathology Conference	5-6 p.m.
3rd Tues.	Dermatology Section Meeting	6-7 p.m.
4th Tues.	Pulmonary Medicine Section Meeting	8-9 a.m.
1st Wed.	Hematology/Oncology Meeting	8-9 a.m.
Every Wed.	Tumor Clinic Conference	2-5 p.m.
Every Wed.	Radiology Conference	5-6 p.m.
	(1) Ultrasound/Nuclear Medicine	
	(2) Radiology Film Review	
	(3) Neuroradiology	
	(4) Teaching File Conference	
	(5) G.I. Radiology	
1st Thurs.	Ophthalmology Section Meeting	7:30-8:30 a.m.
	OB-GYN Conference	8-9 a.m.
	(1) Pathology	
	(2) GYN Analysis	
	(3) OB-Pediatric Combined	
	(4) In-Service and Education	
Every Thurs.	Pediatric Grand Rounds	9-10 a.m.
Every Thurs.	Medical Service Conference	10-11 a.m.
Every Thurs.	Cardiology Conference	11 a.m.-1 p.m.
2nd Thurs.	Orthopedic Grand Rounds	7:45-8:45 a.m.
4th Thurs.	Orthopedic Service Meeting	7:30-9 a.m.
4th Thurs.	Surgical Service Death Review	7:45-8:45 a.m.
Every Thurs.	Psychiatric Service Grand Rounds	10-11 a.m.
4th Thurs.	Urology Section Conference	7:30-8:30 a.m.
Every Fri.	Neurology Grand Rounds	8-9 a.m.

Visiting Professor Program:

2nd Thurs.	Medical Service Visiting Professor	10 a.m.-5 p.m.
2nd Thurs.	Anesthesia Service Visiting Professor	7-8 a.m.
3rd Thurs.	OB/GYN Service Visiting Professor	10 a.m.-4 p.m.
Saturdays	Surgery Service Visiting Professor	8 a.m.-Noon
4th Thurs.	Pediatric Service Visiting Professor	10 a.m.-5 p.m.
as scheduled	Orthopedic Service Visiting Professor	
as scheduled	Family Practice Visiting Professor	
as scheduled	Psychiatric Service Visiting Professor	

All activities have been certified AMA and LCCME Category I. For further information contact James F. Lawsing, III, M.D., Coordinator, Medical Education Committee; 947-3711 Ext. 2303.

A. R. Gould Memorial Hospital Presque Isle, Maine

Every Thurs.	Tumor Conference	8 a.m.
2nd Thurs.	Perinatal Conference	11:30 a.m.
1st and 3rd Fri.	Tumor Conference	

The tumor conferences will be held in the Rotary Regional Educational Center and the perinatal conference will be held in Con-

ference Room A. These conferences have been certified AMA and LCCME Category I. For further information contact Marilyn Dean; 769-2511.

Maine Medical Center Portland, Maine

Every Mon.	Student Technologist Conference	8 a.m.
Every Mon.	Hematology-Pathology Conference	11 a.m.
Every Mon.	Pulmonary Conference	12 Noon
Every Mon.	Pediatric Residents' Conference	1 p.m.
Every Mon.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Mon.	Surgical Pathology Review	4 p.m.
Every Mon.	Radiology Journal Club	5 p.m.
1st & 3rd Mon.	Clinical Nephrology Conference	11 a.m.
1st & 3rd Mon.	Hematology-Pathology Conference	12 Noon
3rd Mon.	Eye Conference	11:45 a.m.
Every Tues.	Radiology Residents' Seminar	7 a.m.
Every Tues.	Family Practice Grand Rounds	9 a.m.
Every Tues.	Electrocardiographic Interpretation	1 p.m.
Every Tues.	Psychiatric Grand Rounds	1:30 p.m.
Every Tues.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Tues.	Surgical Seminar	4 p.m.
Every Tues.	Pathology Slide Seminar	4 p.m.
1st & 3rd Tues.	Radiology-Pathology Conference	12 Noon
1st & 4th Tues.	Neurology Conference	12 Noon
2nd Tues.	Infectious Disease Conference	12 Noon
3rd Tues.	Hematology Conference	12 Noon
5th Tues.	Oncology Conference	12 Noon
Every Wed.	Radiation Therapy Conference	7 a.m.
Every Wed.	Urology Conference	7 a.m.
Every Wed.	Student Technologist Conference	8 a.m.
Every Wed.	Continuing Education Seminar	8 a.m.
Every Wed.	Medical Conference	9 a.m.
Every Wed.	Psychiatric Journal Club	12 Noon
Every Wed.	Cardiology Seminar	12 Noon
Every Wed.	Surgical Grand Rounds	5 p.m.
2nd Wed.	Guest Internist—Medical Conference	9 a.m.
4th Wed.	Medical Mortality Conference	9 a.m.
Alt. Wed.	Neurology-Psychiatry Seminar	11 a.m.
Alt. Wed.	Anesthesiology Journal Club	3 p.m.
Every Thurs.	Thoracic Surgery Conference	7 a.m.
Every Thurs.	OB/GYN Conference	7 a.m.
Every Thurs.	Anesthesiology Clinical Conference	7 a.m.
Every Thurs.	Diagnostic Radiology Teaching Conference	7 a.m.
Every Thurs.	Surgical Conference	8 a.m.
Every Thurs.	Pediatric Conference	9 a.m.
Every Thurs.	Tumor Consultation Board	11 a.m.
Every Thurs.	Medical Residents' Conference	12 Noon
Every Thurs.	Surgical Seminar	4 p.m.
Every Thurs.	Endocrinology Conference	5 p.m.
Every Thurs.	Dental Specialty Lecture	6 p.m.
1st Thurs.	Anesthesia Mortality Conference	7 a.m.
1st Thurs.	Guest Pediatrician	9 a.m.
1st Thurs.	Gastroenterology Conference	12 Noon
1st & 3rd Thurs.	Cardiac-Surgical Conference	12:30 p.m.
1st, 3rd, & 5th Thurs.	Pulmonary-Physiology Conference	12:30 p.m.

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2nd Thurs.	Cardiology Teaching Conference	12:30 p.m.
2nd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
2nd Thurs.	Eye Staff Scientific Session	5:30 p.m.
2nd Thurs.	Maine Medical Center Medical Staff Meeting and Scientific Session	6 p.m.
2nd & 4th Thurs.	Pulmonary-Pathology Conference	12 Noon
2nd & 4th Thurs.	Endocrinology Conference	12 Noon
3rd Thurs.	Combined Guest Pediatrician or Guest Surgeon Program	3 a.m.
3rd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
4th Thurs.	Surgical Mortality Conference	8 a.m.
4th Thurs.	Anesthesia Mortality Conference	3:30 p.m.
Last Thurs.	Pediatric Mortality Conference	9 a.m.
Every Fri.	Thoracic-Surgical Conference	7 a.m.
Every Fri.	Nuclear Medicine Conference	7 a.m.
Every Fri.	Student Technologist Conference	8 a.m.
Every Fri.	Neurological-Neurosurgical Conference	8:30 a.m.
Every Fri.	Gastroenterology Conference	9 a.m.
Every Fri.	Medical Rehabilitation Staff Conf.	9 a.m.
Every Fri.	Orthopedic Conference	9 a.m.
1st Fri.	Dermatology Conference	12 Noon
2nd Fri.	Nephrology Conference	12 Noon
3rd Fri.	Rheumatology Conference	12 Noon
4th Fri.	Oncology Conference	12 Noon
Alt. Fri.	Oncology-Radiation Conference	7 a.m.
Alt. Fri.	Gastroenterology Conference	10 a.m.

All programs have been certified AMA and LCCME Category I. For further information contact Costas T. Lambrew, M.D.; 871-2111.

**Mid-Maine Medical Center
Waterville, Maine**

Every Mon.	Ophthalmology	8-10:30 p.m.
Every Tues.	Tumor Board	12 Noon-1 p.m.
Every Tues.	Regional Infectious Disease ITS presentation	12 Noon-1 p.m.
3rd, 4th, & 5th Tues.	Obstetrics with Augusta General Hospital	12 Noon-1 p.m.
Every Wed.	Regional Pulmonary Disease ITS presentation	12 Noon-1 p.m.
Every Thurs.	Medical-Surgical Conference	12 Noon-1 p.m.
Thurs.-Weekly	Regional Pathology	1-2 p.m.
Thurs.-Monthly	Department of Medicine	6-7:30 p.m.
Every Fri.	Anesthesiology	6:30-7:30 a.m.
Every Fri.	Orthopedics	7-8 a.m.
Every Fri.	Pediatrics	12 Noon-1 p.m.
2nd Fri.	General Surgery	7-8 a.m.

4th Fri. Surgical Audit 12 Noon-1 p.m.
All activities have been certified AMA and LCCME Category I. The Medical-Surgical Conference on Thursday has also been certified AAFP (elective). For further information contact David R. Ginder, M.D.; 873-0621.

**Penobscot Bay Medical Center
Rockland, Maine**

June 27, 1980 **Surgical Grand Rounds**
July 11, 1980 **Pediatric Grand Rounds**
July 25, 1980 **Ophthalmology Grand Rounds**
These grand rounds are from 11 a.m. to 12 Noon and have been certified AMA and LCCME Category I. For further information contact Lloyd Roberts, M.D.; 594-9511.

**St. Mary's General Hospital
Lewiston, Maine**

Every Tuesday Medical Grand Rounds 8-9 a.m.
1st and 3rd Fridays Tumor Conference 12-1 p.m.
Last Friday of month Surgical Grand Rounds 12-1 p.m.
The Surgical Grand Rounds will be alternating monthly between St. Mary's General Hospital and Central Maine Medical Center. These activities have been certified AMA and LCCME Category I. For further information contact Michael C. Bach, M.D.; 783-2227.

**V. A. Hospital
Togus, Maine**

June 20, 1980 **Therapeutic Approaches to Neuropathies** 10 a.m.
Marilyn R. Kassirer, M.D., Staff Neurologist, Veterans Administration Out-Patient Clinic, Boston VA Hospital
Every Wednesday **Medical Staff Service Meetings** 1:15-2:15 p.m.
Every other Thurs. **Oncology Clinic** 2-3 p.m.
2nd Tues. of month **Psychiatric CME Meetings**
These activities have been certified AMA and LCCME Category I. For further information contact E. Osborne Coates, Jr., M.D., VAM and ROC, Togus; 623-8411.

ANNOUNCEMENT: Medical Care Development, Inc. is now receiving a listing of continuing medical education activities taking place in Vermont, New Hampshire, and Massachusetts. If you wish further information contact Gerald Gould, Medical Care Development; 622-7566.

Necrologies

ELLA LANGER, M.D.

1893-1980

Dr. Ella Langer, 86, of Augusta, Maine, died in a Portland hospital on February 2, 1980 following a long illness.

She was born in Vienna, Austria on October 1, 1893, the daughter of Adolph and Eugenia Langer.

Dr. Langer was graduated from the University of Vienna, received her medical degree from the University of Vienna Medical College in 1920, and interned and served a residency at the University Clinic for Children in Vienna.

From 1944 to 1965, Dr. Langer was Director of the Division of Maternal and Child Health and Crippled Children's Service of the Department of Health and Welfare in Augusta. She served as

visiting lecturer at Harvard University School of Public Health and as Research Fellow at Johns Hopkins University. After her retirement, she became a pediatric consultant for the Head Start program.

An honorary member of the Kennebec County Medical Association and the Maine Medical Association, Dr. Langer received a 50-year pin in 1970 and a 55-year pin in 1975. She was also a diplomat of the American Board of Pediatrics and the American Board of Preventive Medicine, and was an honorary staff member of the Central Maine Medical Center in Lewiston.

She is survived by several cousins.

C. EUGENE FOGG, M.D.

1882-1980

Dr. C. Eugene Fogg, 97, of Portland and Peaks Island, Maine, died on February 9, 1980 in a Portland hospital after a brief illness.

Born in Portland, Maine on December 27, 1882, he was the son of George and Octavia Fogg.

Dr. Fogg was graduated from the Massachusetts Institute of Technology, received his medical degree from Bowdoin Medical School in 1914, and interned at the Maine General Hospital in Portland.

Dr. Fogg served in the military from 1917 to 1947, retiring with an honorary rank of Brigadier General from the Medical Corps, Maine National Guard in 1947. He was Senior Medical Officer, U.S. Naval Station, Hingham, Massachusetts in 1917; Surgeon, U.S.S. Sierra in 1918; Assistant Surgeon, U.S. Naval Hospital, Portsmouth, New Hampshire in 1919; Brigade Surgeon, First

Naval District, 1920-1928; Battalion Surgeon, 240th Coast Artillery, Maine National Guard, 1930-1932; Regimental Surgeon, 240th Coast Artillery, Maine National Guard, 1932-1942; and Professor of Military Medicine, Army Training Schools, University of Vermont College of Medicine, 1942-1945. He located in Peaks Island following his retirement.

An honorary member of the Cumberland County Medical Society and the Maine Medical Association, he received a 50-year pin in 1964, a 55-year pin in 1969, a 60-year pin in 1974 and a 65-year pin in 1979. Dr. Fogg was also a member of the American Medical Association and the Cumberland Barracks of the Veterans of World War I.

He is survived by his widow, the former Ethelynn Steele of Portland.

FRANCIS H. FOX, M.D.

1916-1980

Dr. Francis H. Fox, 64, of Portland, Maine, died on February 26, 1980.

He was born in Portland, Maine on January 7, 1916, the son of Frank and Alice Fox.

Dr. Fox was graduated from Holy Cross College and received his medical degree from Columbia University College of Physicians and Surgeons in 1941. He interned and served a residency at the Kings County Hospital in Brooklyn, New York, and took postgraduate courses at the University of Pennsylvania, Columbia

University and Albert Einstein Medical School.

During World War II, he served in the U.S. Air Force as a Major.

In 1948, he located in Portland where he was affiliated with the Maine Medical Center and the Mercy Hospital.

Dr. Fox was a member of the Cumberland County Medical Society, the Maine Medical Association and the American Board of Pediatrics.

Surviving is his widow, the former Catherine Cahill of Portland.

COUNTY SOCIETY NOTES—Continued from Page 165

mented on the plan, stated that suggestions made by the medical profession, who are members of HSA were always a minority report, since consumers formed the main part of the HSA. Suggestions that he and other doctors made were not carried out.

Motion was made and seconded by Dr. Robertson that the Washington County Medical Society lend their support to any legal action that the Executive Committee of the Maine Medical Association proposes to take toward an injunction against hasty adoption of the State Health Plan. This motion was passed.

There was further discussion of the affects of this plan on practice now, and in the future, and its affect on attracting physicians to the area.

It was generally felt that the proponents of this type of plan

generally favored centralization and had little thought to rural areas. The larger hospitals in the State would benefit from a plan of this type, where things were more centralized and it would be more favorable to them but a further loss to rural areas.

It was suggested that due to the size of Washington County that the County Society could be divided into two sections, Eastern and Western, with the Eastern centered in Calais and the Western in Machias; each to meet as desired, with at least one annual meeting of the whole group, once or twice yearly.

This was not acted on, but will provoke further discussion.

IV. Meeting adjourned at 8:55 p.m.

KARL V. LARSON, M.D., Secretary

News, Notes And Announcements

Five Year Focus—Orthotics/Prosthetics

The Department of Orthotics and Prosthetics at Eastern Maine Medical Center recently completed its fifth year of service to the community. We have been successful in our goal and purpose of improving the quality and availability of orthotic and prosthetic services to clients in northern and eastern Maine.

To meet the needs of our growing service area, the department now has eight employees, including three orthotist/prosthetists who provide consultant services at 15 clinics each month throughout the area from Rockland to Caribou. This represents a shared service concept providing physicians and hospitals in other communities with up-to-date expertise on a regular basis.

Continuing to pursue our goal of improving orthotic and prosthetic services to Maine, we now are offering an educational program to medical and rehabilitative personnel which acquaints them with modern techniques and materials.

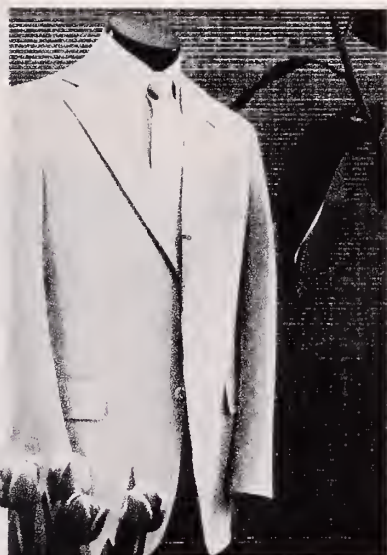
This cooperative effort, we believe, will result in improved patient care.

INQUIRIES: Mark C. Picurro, C.P.O., Director, Orthotics/Prosthetics, Tel. (207) 947-3711, extension 2454.

Maine Society for the History of Medicine

The Society meets five times a year in various locations throughout the State. Medical historical presentations include addresses, lectures, papers and discussions, as well as viewing historical sites. Original research is encouraged.

Membership is open to any person or institution interested in the history of medicine. Annual dues are \$5.00 for an individual and \$25.00 for an institution. Interested persons may obtain additional information by writing to the president of the society, Richard J. Kahn, M.D., Pen Bay Physicians Building, Rockland, Maine 04841.



Spring is Here!

Time to Suit Up for the Spring Season. At David Wood the Spring Collection of Fine Suits has arrived. The Collection includes a choice selection of styles and patterns including all of these Traditional Favorites:

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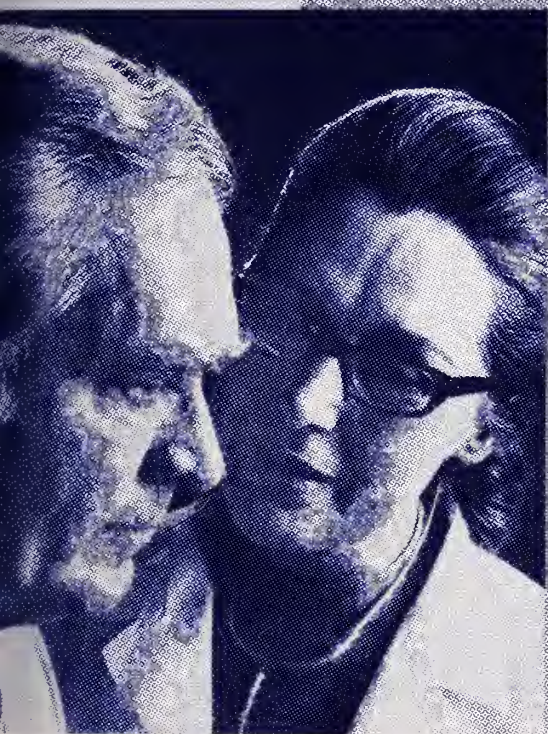


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County Society Notes

York

The annual meeting of the York County Medical Society was held on January 9, 1980 at the Kennebunk Inn in Kennebunk.

A social hour was held from 6:30-7:30 p.m. Following this, a superb dinner was served. The next item on the agenda was a talk by Dr. George Sullivan, Secretary of the Maine State Board of Registration in Medicine. His subject was "The Maine State Board of Registration in Medicine." He was introduced by Dr. Conner M. Moore, our President. He presented a most comprehensive and interesting speech on its history from its inception, up to the present. His talk met with the approval and satisfaction of all members of our Society present. Questions and answers were presented throughout its entirety.

Following this, the business meeting was called to order by our President. The report of the nominating committee was then given and consisted of the following slate of officers and committee for 1980:

President: Dr. Conner M. Moore, Biddeford

Vice President: Dr. Irvin Dorfman, Sanford

Secretary-Treasurer: Dr. Melvin Bacon, Sanford

Executive Committee: Drs. Kenneth E. Leigh, York, Maurice Ross, Saco and Robert D. Vachon, Sanford

Delegates to the M.M.A. House of Delegates: Drs. Carl E. Richards, Alfred, Irvin Dorfman, Sanford and Ruth E. Endicott, Ogunquit. Alternates: Drs. John H. Leonard, York, Thomas M. Collins, Sanford and Donald G. Belliveau, Biddeford

Censors Committee: Drs. Marion K. Moulton, W. Newfield, Thomas Anton, Biddeford and Roger J.P. Robert, Biddeford
Peer Review: Drs. Arthur E. Spearing, Jr., Springvale, Carl M. Haas, Biddeford and Mirle A. Kellett, York Harbor

Arbitration Committee: Drs. Richard S. Tockman, Sanford, Lawrence R. Hazzard, York and Owen O. Dow, Kennebunk

Membership Committee: Drs. David L. Massanari, Sanford, Conner M. Moore, Biddeford, Alexander W. Magosci, York and Carl E. Richards, Alfred

Nominating Committee for 1981: Drs. Melvin Bacon, Sanford, Leopold A. Viger, Biddeford and Alvin A. Hoffman, York

This slate of officers and committees was unanimously voted into office by the members present.

The minutes of the October meeting were dispensed with in the interest of time. The financial report for 1979 was then given. It was announced that we are financially in good shape, and that our dues are among the lowest in the State. Barring unforeseen events, no increase in county dues is contemplated, and expenses have been kept at a minimum.

There was no old business to present.

Under new business, the presentation of the applications of the following physicians to the York County Medical Society for membership: Drs. David Rowden, John Truslow, James W. Georgitis, Nick Kalamaras and Harendrababu Patel.

These were unanimously elected into membership.

A report of the House of Delegates Meeting was given by Dr. Irvin Dorfman, which was held Saturday, November 17, 1979, at the Mid-Maine Medical Center in Waterville. The various items on the agenda were presented in brief, with the exception of the report of the Health Care Finance Committee, on which he put much emphasis regarding negotiations with Blue Cross-Blue Shield.

After this presentation, it was unanimously voted by our Society to approve of the action of this committee, as well as the House of Delegates.

Next on the agenda were announcements. These included the March 12th meeting to be held in the Sanford area with place to be announced. The committee in charge consisted of Drs. Melvin Bacon, Carl Richards and Robert Vachon. Other items in this category were a program on arthritis and rheumatology to be held at Nason College in the Spring or Fall of 1980, and also a series of three-day sessions to be held during the Summer of 1980, pending further arrangements.

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Number 7

Legionnaires' Disease

Recognition of the Togus Strain

ROBERT I. WISE, M.D., PH.D., F.A.C.P.*

Legionnaires' disease was first recognized in an outbreak in Philadelphia in the summer of 1976.¹ A bacterium was isolated from the lung tissues of four fatal cases by inoculation of guinea pigs intraperitoneally.² Indirect fluorescent-antibody tests of acute and convalescent sera of survivors revealed a high proportion of seroconversion to the agent. Conventional staining methods failed to demonstrate the presence of the bacteria in lung tissue and sputum; however, the silver-impregnation stain of Dieterle showed the microorganisms to be present in large numbers in lung tissue and to be morphologically identical to those seen in the peritoneal exudates of inoculated guinea pigs.³ These observations seemed to prove the etiologic role of the bacterium and to explain why the microorganism had not been observed in tissues and sputum of patients with pneumonia which had been caused by this agent in the past.

Since these reports were published, there have been investigations of other epidemics and sporadic cases of this disease, some occurring prior to and some after 1976 as has been reviewed by Sanford.⁴ Investigators have attempted to discover the environmental sources of the agent and explain its mode of transmission. During an epidemic in Bloomington, Indiana in 1978, the bacterium was isolated from water in a cooling tower and a nearby stream.⁵ An outbreak at a hospital in Memphis, Tennessee in 1978 was associated with contamination of water in an air conditioning cooling tower, which suggested an air borne mode of spread.⁶ The microorganism has been found with increasing frequency in streams and soil^{7,8} and has been shown to remain viable in water for as long as one year.⁹ Evidence indicates that the bacterium of Legionnaires' disease, *Legionella pneumophila*, is ubiquitous in the environment, and can contaminate evaporative con-

densers and cooling towers; however, the epidemiology of sporadic cases in the environments without air conditioners and cooling towers remains obscure.

Legionnaires' disease was first recognized at the VA Medical Center at Togus, Maine in April 1978. From lung tissue, which was obtained post mortem and submitted to the Center for Disease Control, a bacterium was isolated and subsequently identified as a new serogroup of the Legionnaires' disease bacterium. This newly recognized strain became known as the Togus strain, and is identified as *Legionella pneumophila*, serogroup 2.

At least four distinct serogroups of *L. pneumophila* are now recognized; the reference strain (Knoxville) which is related to the Philadelphia strain, the Togus strain, the Wadsworth VA strain and a strain recovered from creek water in Bloomington, Indiana.¹⁰

It is the purpose of this report to describe the clinical and microbiologic events which led to the discovery of the Togus strain and to present evidence that the Togus strain has been existent for a number of years prior to its recognition in 1978. The following three case reports (Togus cases 1, 3 and 6) are pertinent to this understanding.

CASE REPORTS

Case 1: The patient, from whom the first isolation of the Togus strain was made, was a 30-year-old male veteran who was admitted for treatment of a psychiatric illness on November 30, 1977. He was a smoker of one package of cigarettes per day, had been treated for pulmonary tuberculosis from 1970 to 1973, and had suffered episodes of gastritis with reflux esophagitis since 1974. He improved and returned to his home on March 31, 1978. The next day he developed anorexia, malaise, fever, chills, muscle aches, and a non-productive cough. He returned to Togus on April 2, 1978. During the next three days his temperature ranged from 102 to 105.4°F, pulse from 84 to 144 per minute, respirations from 20 to 48 per minute and blood pressure from 140/40 to 140/80. He was confused. Respiratory rales were heard over the left hemithorax. Laboratory studies revealed the following pertinent data: Hb. 14.1 grams, hct 41.5%, WBC 18,000 per cu. mm with

*Chief of Staff, VAM & ROC, Togus, Maine 04330.

neutrophilia of 91% and a left shift, 4+ proteinuria, arterial blood: pH 7.56, PCO₂ 20.5 mmHg, PO₂ 53 mmHg, bicarbonate 18.2 mEq per liter, oxygen saturation 93%. Examination of a purulent sputum by Gram stain revealed polymorphonuclear leucocytes in clusters with a mixture of Gram positive cocci in short chains, pairs and groups, Gram negative cocci and a few Gram positive bacilli. A culture of the sputum demonstrated alpha hemolytic streptococci and a few colonies of *S. pneumoniae*. A blood culture revealed no evidence of bacteremia. Roentgenograms of the chest showed no evidence of pneumonia on April 2, 1978; however, a rapidly developing infiltrative consolidation of the left lung was evident on April 4, 1978. The patient died on April 5, 1978, three days following his return to the hospital. Postmortem study revealed bilateral hemorrhagic pneumonitis with pulmonary edema. Specimens of lung tissue were submitted to the C.D.C. to determine the presence of Legionnaires' disease.

Case 3: A 31-year-old male who was a cigarette smoker was admitted on April 20, 1978 for treatment of a psychiatric illness. He improved and was sent home on May 19, 1978, only to return four days later on May 23, 1978 with symptoms of anorexia, malaise, fever and chills. There was physical evidence of pneumonia of the right lower lung. Roentgenograms, which were reported as normal on April 24, 1978, revealed a dense process in the right lower lung field and extending into the right upper lobe on May 23, 1978. On May 24, 1978, the process involved the entire right lung and was beginning to involve the left lung. The patient was treated with erythromycin 500 mg. every six hours intravenously for nine days with recovery. Specimens of acute and convalescent sera were submitted to the C.D.C. for confirmation of the diagnosis of Legionnaires' disease.

Case 6: A retired employee of the VA Medical Center at Togus developed fever, chills and headache while at work on November 24, 1971 when he was 49 years of age. He had smoked one package of cigarettes per day for 30 years. He was seen by a physician, who prescribed a medication. He became progressively worse and was admitted to the Gardiner General Hospital where it was determined that he had pneumonia. He developed severe hemoptysis, melena, with oliguria and azotemia. On November 30, 1971, the patient was transferred to the VA Medical Center at Togus for hemodialysis and was treated with blood transfusions and intravenous cephalothin, 1 gram every four hours and carbenicillin, 2 grams every four hours. The patient recovered and was discharged from the hospital on February 9, 1972. A specimen of serum was obtained on December 20, 1978, approximately seven years following the illness, and submitted to the C.D.C. for titration of antibodies to Legionnaires' disease bacillus.

RESULTS

The results of studies of the specimen obtained from case 1 were reported by the C.D.C. to Togus on April 27, 1978. Moderate numbers of microorganisms typical of Legionnaires' disease were observed in the lung tissue. The bacterium was isolated in guinea pigs and cultured on agar from the guinea pig tissue. Later reports on July 10, 1978 indicated that both patients (cases 1 and 3) had suffered Legionnaires' disease caused by a new serogroup of the bacillus. Identification of the new serogroup was announced by the C.D.C. in the morbidity and mortality report of August, 1978.¹¹ The procedures which were used at the C.D.C. in identifying this microorganism have been described previously.^{2,3}

The bacterium (Togus strain) which was recovered from the lung tissue of case 1 reacted negatively to tests for direct fluorescent antibody staining with fluorescein isothiocyanate conjugates of antibodies produced in rabbits against 16 other strains of Legionnaires' disease bacilli. Fluorescein labelled antibodies produced in rabbits against the Togus strain stained bacteria of the Togus strain, but did not stain

TABLE 1

TITERS OF ACUTE AND CONVALESCENT PHASE SERA OF CASE 3 UTILIZING INDIRECT FLUORESCENT ANTIBODY STAINING

Bacterial Strains	Serum Case 3		Control Serum
	Acute	Convalescent	Detroit Convalescent
Philadelphia 1	1-32	1-256	1-262,144
Detroit	1-32	1-256	1-262,144
Case 1 (Togus)	1-32	1-8,192	1-128

the bacterial cells of the other 16 strains of Legionnaires' disease bacillus. These results indicated a dissimilarity of antigenic structure of the Philadelphia and Togus strain.

The titers of the acute and convalescent phase sera of case 3 were determined by using the indirect fluorescent antibody staining of bacterial cells of the Philadelphia 1, Detroit and Togus strains as antigens. A specimen of convalescent serum obtained from a patient with Legionnaires' disease in Detroit was used as a positive control. The results of these studies are shown in Table 1.

It can be seen that the rise in titer from 1-32 to 1-256 to the Philadelphia 1 antigen in the sera of case 3 indicated a recent infection with the Legionnaires' disease bacillus. The greater rise in titer from 1-32 to 1-8,192 to the Togus strain isolated from case 1 indicated that the patient of case 3 had probably been infected with the Togus strain of case 1. The antigenic difference between the reference strain and the Togus strain is also indicated by the titer of 1-128 of the Detroit convalescent serum, when tested with the Togus strain, and the titers of 1-262,144 when tested with the Philadelphia and Detroit antigens. It is evident from these observations that the Togus strain is a Legionnaires' disease bacillus and is a different serogroup than the Philadelphia strain.

The specimen of serum, which was obtained from the retired employee of Togus, case 6, seven years following a severe illness was reported to react positively in a titer of 1-128 to the Philadelphia strain and 1-512 to the Togus strain. It is presumed that his illness of 1971 was Legionnaires' disease; however, this conclusion cannot be confirmed. This is evidence of previous infection by the Togus strain in years prior to its recognition in 1978.

DISCUSSION

Since the recognition of Legionnaires' disease at Togus in April 1978, the diagnosis of this disease has been confirmed in seven patients and a presumptive diagnosis has been made in one patient. Of the eight cases, seven have been caused by *L. pneumophila*, a serogroup 2 (Togus strain) and in one patient, *L. pneumophila* serogroup 1 (Knoxville strain) was the etiologic agent. The occurrence of these infections have been sporadic with four cases recognized in 1978 and four cases in 1979. Studies to determine the epidemiology of these sporadic cases are in progress.

Continued on Page 214

Parathyroid Carcinoma

A Case Report and Review

JOHN W. STURZENBERGER, M.D., DANIELLE MUTTY, M.D., HENRY B. PERRY, M.D., PH.D.
AND WILFRED GUERRA, M.D.*

Heath and his colleagues have suggested that the use of the automated multichannel blood chemistry analyzer has resulted in an increased recognition of hypercalcemia and primary hyperparathyroidism.¹ In the majority of these cases, the etiology is an adenoma of the parathyroid gland. Diffuse hyperplasia of all four glands accounts for a second major fraction.^{2,6} The remainder of the cases, estimated at from 1-5%, are caused by the presence of a hyperfunctioning parathyroid carcinoma.^{3,4} Since the number of cases discovered is increasing and the advisability of surgery in mild primary hyperparathyroidism is currently being discussed,⁵ it is worthwhile to review the characteristics of parathyroid malignancy and emphasize the features which may alert the clinician to its possible presence.

A representative case of parathyroid carcinoma will be reported and the pertinent features of the disease, its diagnosis, and treatment will be presented. The apparent affect of propranolol on the serum calcium and parathyroid hormone level will be noted.

CASE REPORT

A 66-year-old man was admitted to the Togus VA Hospital on December 23, 1979 for evaluation of confusion and combative behavior. He had had labile hypertension for over 35 years. In recent years this had required treatment with a multidrug regimen, which included propranolol. Diabetes had developed 10 years prior to admission and he had recently required a small dose of long acting insulin. In retrospect, he recalled passing a large kidney stone about 15 years earlier. About the same time all his teeth had fallen out. He passed no further kidney stones and experienced no bone pain. However, he was known to be hyperuricemic and had experienced at least one episode of colchicine responsive acute gout. Some 10 to 15 years prior to admission he had had a tumor removed from the surface of the top of his head. It had recurred after several years. There was a family history of hypertension, "stomach cancer," and non-crippling arthritis. He had been evaluated by a physician in early December 1970 for mild asymptomatic hypercalcemia. A parathyroid hormone level drawn at that time was not elevated. Shortly after this time the patient sustained several rib fractures in a fall. When pneumonia developed, antibiotics were prescribed and codeine was added for pain. The patient later stated, "I went out of my head." The family confirmed that he had been confused and agitated and had threatened them. Admission to our hospital had then been arranged.

When first seen he presented as a well developed man looking his stated age, who was drowsy and slept alot. Intermittently, he complained of headache, weakness, and thirst. The BP was 170/120. The pulse ranged between 50 and 80 with periods of junctional escape rhythm noted on the cardiac monitor. The weight was 20 pounds below his normal weight. He was afebrile. Diffuse freckling was noted on the back, shoulders, arms, and hands. An 8 cm by 5 cm circumscribed semifirm mass of the top of the head was noted. The mouth was dry. The voice was noticeably coarse.

No masses were palpable in the neck. There was no lymphadenopathy. The auscultation of the heart was normal. The liver and spleen were not palpable. The muscle strength in the proximal muscles was weak, but his grip strength was unimpaired. The reflexes were normal.

Shortly before coming to Togus, the patient's serum calcium was 11.5. Over the next several days, it rose to 15.4. Several serum phosphorus determinations were less than 2.5. Inappropriate phosphaturia was demonstrated. Urine calcium excretion was normal. The BUN was slightly elevated but the creatinine was normal. The serum alkaline phosphatase level and serum chloride were normal on admission, but later rose. Parathyroid hormone levels were 1.5 to 4.5 times the upper limit of normal for the assay. Bone films showed only diffuse osteoporosis. An IVP was normal. There was no evidence of a mass lesion in the chest, upper GI tract, colon, or rectum. A clinical diagnosis of primary hyperparathyroidism was made and a neck exploration was performed.

OPERATIVE REPORT: FINDINGS

A routine collar incision was made through all layers of skin, subcutaneous tissue and fascia, and platysma muscle. The flaps were freed, superiorly to the superior laryngeal notch and inferiorly to the sternal notch. Next the cervical fascia was divided in midline. Exposure was enhanced by appropriately dividing the strap muscles bilaterally between muscle clamps.

The right thyroid lobe was of average size and of uniform consistency. The isthmus presented a minor anomaly in that it continued as the lower pole of the right lobe, turned sharply and continued obliquely upward across the trachea to join the medial lower segment of the left lobe. The right inferior recurrent laryngeal nerve was identified and traced, the tracheo esophageal groove was visualized. The jugular vein and carotid sheath were traced and no masses or lymph nodes were observed. Exploration was limited posteriorly to the anterolateral ridges of the transverse processes of the cervical vertebrae.

Search for parathyroid glands progressed by freeing up some of the right thyroid lobe. The vessels at the inferior pole, invested in loose thyroid tissue, were divided between clamps and the pedicles were ligated with 3-0 silk. Also the isthmus was divided between clamps. It was then possible to roll the thyroid medially and laterally. Exploration of the right side of the neck proved negative for parathyroids, nodules, and lymph nodes. Small fragments of lobular fibroadipose tissue obtained from the pretracheal fascial plane were submitted for frozen section and were reported negative for parathyroid cells.

The left side of the neck was explored in similar manner and it was unrewarding until attention was focused on the left thyroid lobe. It appeared larger than the right. The capsule over the body of the lobe was smooth, but uneven; and the gland was irregular by comparison.

On the basis of these findings and the significant laboratory test, the final surgical step was directed to doing a total left thyroid lobectomy. The upper pole of the lobe was freed by dividing the superior thyroid vessels between clamps and ligating with 3-0 silk. The lobectomy was accomplished by dissecting the gland off the pre-tracheal fascia medially to laterally. As the posterior aspect of the lobe came into view, a nodule 5-6 mm in diameter presented itself just below the junction of the upper pole and body of the lobe. It appeared to penetrate the posterior capsule of the gland, but there was no gross invasion of the skeletonized trachea surface. The nodule was surrounded by tiny irregular hemorrhagic streaks that varied from red to reddish-green in appearance. After removing the left lobe, a tissue specimen was sent for frozen section. It was found to be parathyroid tumor. The tumor invaded the

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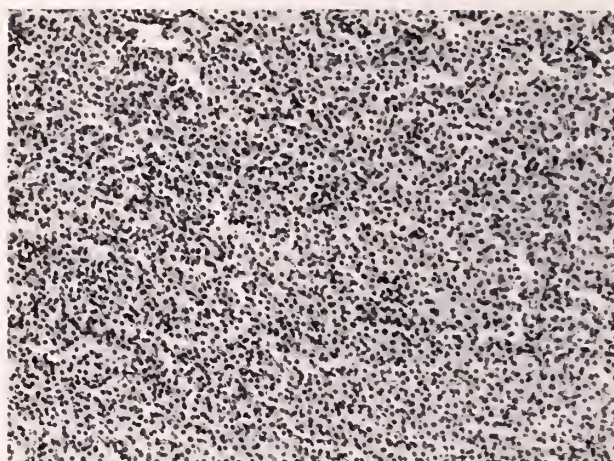


Fig. 1. 160X—Low power view of tumor cells.

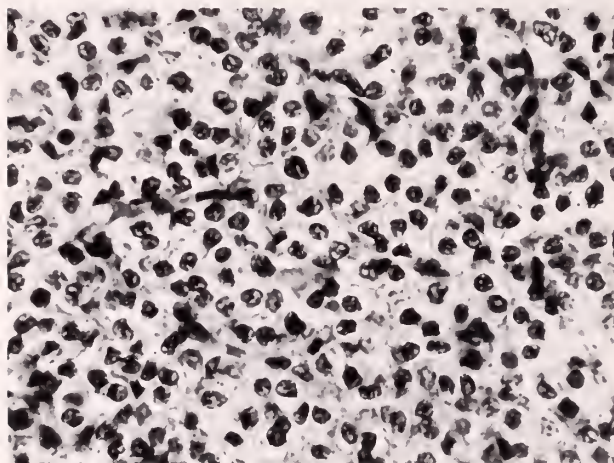


Fig. 2. 400X—Higher magnification of tumor cells.

substance of the thyroid gland and it was impossible to determine its dimension or weight.

DESCRIPTION OF THE PATHOLOGY

Gross: Received in the pathology laboratory for frozen section were four fragments of tissue from the right and left neck for identification. No parathyroid tissue was identified in these sections. The main specimen consisted of a left thyroid lobectomy. A frozen section from a posterior nodule revealed a parathyroid tumor. The left portion of the thyroid gland weighed 10 grams and measured 3.8 x 2.4 x 1.4 centimeters. A rubbery lesion (from which the frozen section had been submitted) was felt near one edge measuring 1.5 x 1.4 x 0.6 centimeters. A small nodule measuring 0.6 centimeters in diameter was also noted near the above. The remainder of the thyroid gland appeared unremarkable. On cut section, the thyroid tissue was reddish and firm and the two masses were light tan and rubbery.

Micro: The tumor was composed of chief cells with round regular nuclei, occasional mitotic figures, pale eosinophilic and well defined cytoplasm (Fig. 1 and Fig. 2). Hyalinized connective tissue and blood vessels were noted throughout separating groups of cells (Fig. 3). Hemosiderin pigment and focal hemorrhage were prominent. The tumor in some areas invaded thyroid tissue and a definite capsule could not be identified in these areas (Fig. 4). Papillary arrangement was seen in some areas of this tumor. The thyroid acini and stroma appeared essentially unremarkable. Ultrastructural studies were done (Fig. 5 and 6).

Diagnosis: Parathyroid carcinoma, left, extending into the left thyroid gland. Note: Representative sections were sent to the Armed Forces Institute of Pathology, Washington, D.C. and the diagnosis of parathyroid carcinoma was confirmed.

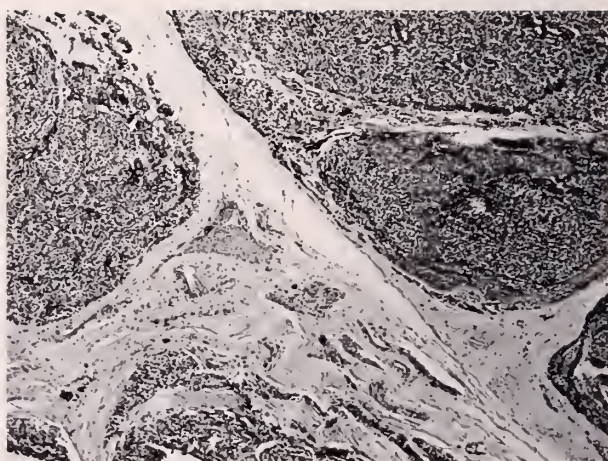


Fig. 3. 40X—Broad bands of collagen between tumor cell nests.

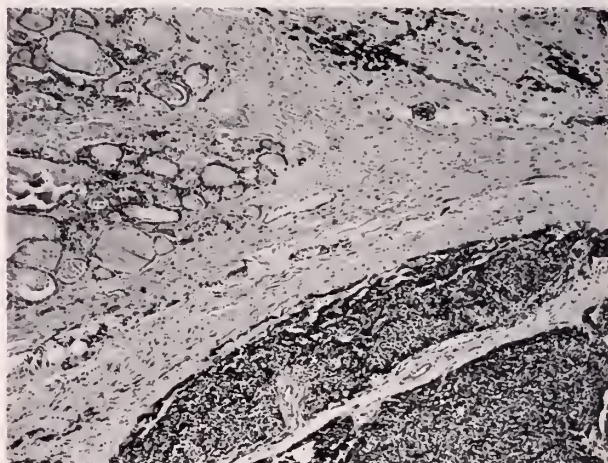


Fig. 4. 40X—Relationship between tumor and thyroid. Note vascularity of fibrous band between the thyroid tissue and parathyroid tumor.

Postoperative course: Postoperatively the serum calcium fell to 6.1 and the parathyroid hormone level (Fig. 7) became normal. A search for metastases showed no evidence of either pulmonary or hepatic lesions. A CT head scan defined a calcified intracranial lesion as a probable meningioma. Spinal fluid pressure, protein, PTH and fractionated catecholamines were not elevated. A 24^{hr} urine collection for catecholamines, V.M.A. and metanephrone was normal. Serum calcitonin was not detectable. Prolactin, ACTH, growth hormone, and gastrin levels were normal. A sonogram showed no detectable adrenal or pancreatic tumor. A radionuclide scan of the liver and spleen showed the absence of uptake in the upper portion of the spleen thought to be consistent with infarction. Normal postoperative calcium and PTH values were against this being a functioning metastasis. A dermatologic consultant evaluated the patient and felt that the patient had no evidence of axillary freckling and the pigmented lesions which he did have were too small and too few to diagnose von Recklinghausen's disease. The patient's densely calcified intracranial lesion is considered stable and will be followed with serial x-rays.

DISCUSSION

In reviewing 732 cases of primary hyperparathyroidism, Castleman and Roth noted that adenomas comprised 81%. There were 15.4% with diffuse hyperplasia of all four glands and 2.9% were carcinomas.⁶ A second primary neoplasm was not reported. It is noteworthy however, that in other

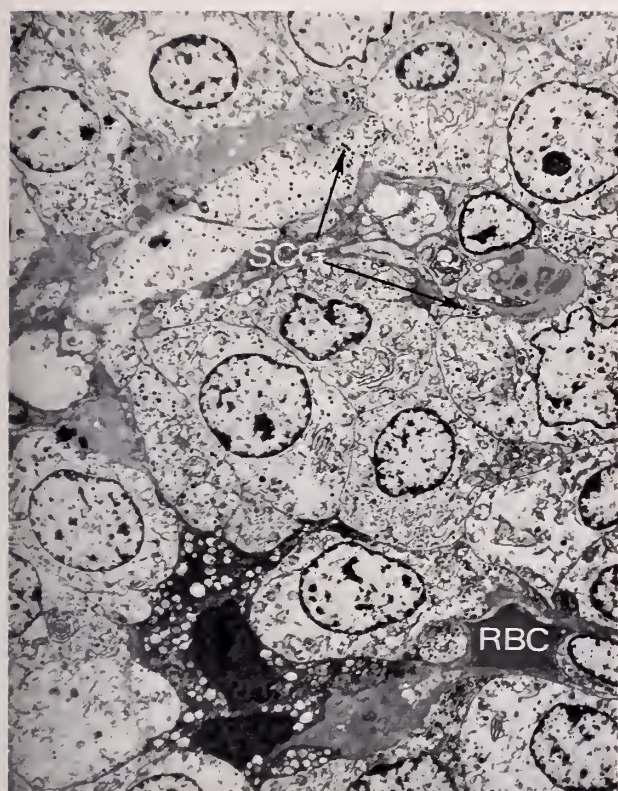


Fig. 5. 4,000X—SCG, secretory granules; RBC, red blood cells.

series the diffuse hyperplasia group is dominated by the chief cell variety⁶ and 18% of these patients have the syndrome of multiple endocrine neoplasia (MEN).⁷ While no cases of parathyroid carcinoma have been reported with MEN it has developed in the setting of chief cell hyperplasia associated with familial hyperparathyroidism.⁶

A collective review of the previously reported 46 cases of hyperfunctioning parathyroid carcinoma was prepared by Holmes in 1969.⁹ He documented a 60% male predominance and a prevalence in the 30-50 year old age group (66%). The clinical course was shown to be related to the effects of severe hypercalcemia: extreme weakness, mental depression, psychosis, weight loss, anemia, cardiac irregularities, thirst, anorexia, nausea, vomiting, constipation, and vague abdominal pain. Renal disease developed in 32%, pancreatitis in 15% and bone disease in 73%. While the literature suggested that these were slowly growing, late metastasizing tumors, 52% had metastasized at presentation (cervical, lung, liver, pancreas and adrenals). The cause of death was due most often to the metabolic effects of hyperparathyroidism (uremia, cardiac arrhythmia and wasting). The preoperative diagnosis of carcinoma was said to be favored by a very high serum calcium (average 15.9), a palpable mass in the neck, vocal cord paralysis, and hypercalcemia that recurred after surgery. Intraoperatively, the hard, white, densely fibrous, locally infiltrating carcinoma was said to be distinguishable from the soft, reddish brown adenoma.⁹ Parathyroid hormone levels have recently

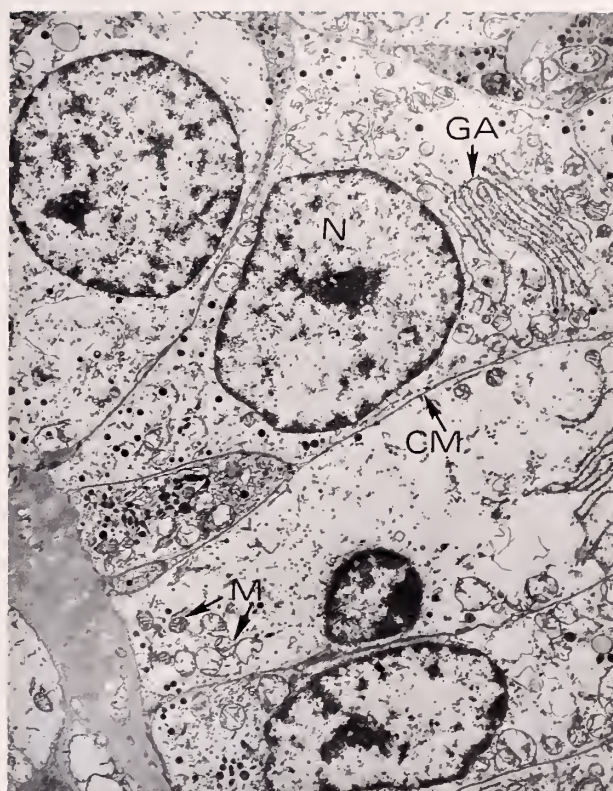


Fig. 6. 14,500X—GA, golgi area and rough endoplasmic reticulum; N, nucleus; CM, cell membrane; M, normal and degenerated mitochondria.

been reported in 3 cases and these show some correlation with tumor size.¹⁰ The hyperfunction of these tumors was felt to be consistent with the low grade nature of the malignancy (Purnell, 10).

In 1973, Shantz and Castleman analyzed 70 cases of parathyroid carcinoma accumulated in a single diagnostic center over a 33-year period.³ While the basic clinical elements described in Holmes' study were confirmed, the incidence of a palpable neck mass, metastases and recurrence were apparently lower.

This paper included detailed pathologic data on the cases analyzed. Grossly, the tumors weighed from 0.5 to 42.5 grams with a 12.0 gram average.³ They did not attempt to relate tumor size to outcome. However, in two more recent papers reporting tumors 0.5 to 9 grams and 2.5 to 16 grams respectively, tumor weight did not correlate with the incidence of metastases or death.^{4,10*} Evaluation of the diagnostic criteria for histologic diagnosis has shown that 90% of the specimens demonstrated fibrous trabeculae, 81% mitotic figures, 67% capsular invasion, and 12% had vascular invasion. A bland, rather uniform cell pattern was characteristically described.³ Van Heerden has recently emphasized the fact that the cells of a carcinoma were larger than chief cells and were characterized by abundant clear or eosinophilic cytoplasm.¹⁰ Ultrastructural studies

*Graphic analysis of author's data

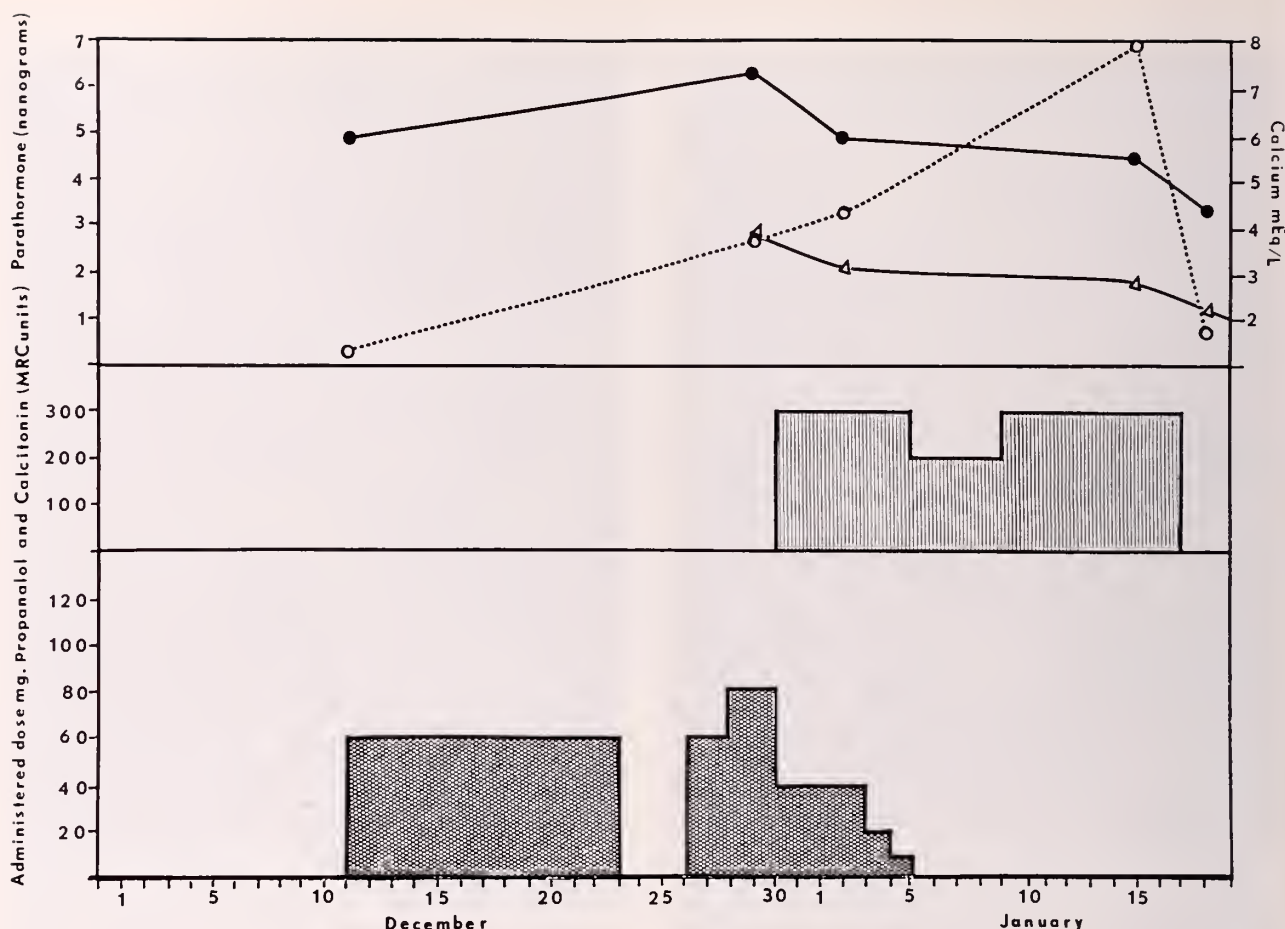


Fig. 7. The above graph shows that the patient's serum calcium was only mildly elevated on 12/11/79. The next calcium and PTH levels were drawn after the patient was without propanolol for at least three days. A further rise corresponded with the hypocalcemic effect of calcitonin. Given are the total daily administered doses of propanolol and calcitonin (MRC units). ●—● total serum calcium (normal range 4.4-5.2 mEq/L); △—△ ionized serum calcium (normal range 2.2-2.52 mEq/L); ○---○ parathormone level (normal range 200-1500 pg/ml). Surgery performed on January 17.

of 3 cases of parathyroid carcinoma have shown large cells with complicated interdigitating plasma membranes, virtually absent desmosomes, abundant rough endoplasmic reticulum, prominent golgi, pleomorphic nuclei and a prominent nucleolus. This was felt to reflect the high degree of metabolic activity of the cells and correlates well with the serum calcium.¹³ None of the cases described by Shantz and Castleman showed evidence that the carcinoma had arisen from an adenoma or hyperplasia.³ Castleman has recently pointed out that the latter may occur.⁶ The histologic differentiation of adenoma from low grade malignancy may be difficult.^{10,14}

The therapy of parathyroid carcinoma remains surgical.^{4,5} Holmes⁹ recommended total excision of the tumor and removal of the thyroid isthmus and ipsilateral lobe. Skeletonization of the trachea and excision of any skeletal muscle intimately related to the tumor was advised. He suggested that the recurrent nerve be resected if involved, as dissection resulted in recurrences. Surgeons were cautioned to avoid rupturing the capsule. Holmes advised removal of the nodes in the tracheoesophageal groove and an ipsilateral radical neck dissection as a way to prevent metastases. The need to do such a procedure has

recently been questioned.^{4,10} Purnell has stated that 70% of cases operated on for hyperparathyroidism are asymptomatic with mild hypercalcemia picked up on serum biochemical screening. He has emphasized early recognition as the key to improving surgical therapy.¹⁰ In addition, he has underscored the important role of the surgeon in recognizing the lesion and then performing a careful excision, thus preventing metastases.

Seventy-seven percent of the patients dying of their disease died of the effects of hyperparathyroidism and not because of replacement of organs by tumor.³ Holmes advised that the metabolic effects of recurrent tumor be controlled by palliative local resection.⁹ Radiotherapy has not been effective.^{9,10} Two cases were said to have had some palliative benefit from estrogens⁹ but a recent discussion makes no mention of its use.¹⁰ Thyrocalcitonin^{16,17} and mithramycin¹⁸ have been effective in controlling hypercalcemia. The use of parathyroid hormone analogs which block the normal PTH induced release of cyclic AMP from target organs is under investigation.²⁰ Propanolol which blocks B adrenergic stimulation of PTH secretion has been shown to be effective in the control of PTH and serum calcium

levels in some patients with primary hyperparathyroidism.^{11,15} The use of B adrenergic antagonists may help to control the effects of functioning metastatic tumors in the future.

The case presented in this report is noteworthy in that despite evidence of disease for at least 15 years, a palpable mass was not present and the serum calcium was only mildly elevated. For the most part, the patient's course had been asymptomatic. His lack of symptoms and the mildness of his hypercalcemia may have been due in part to suppression of his PTH and serum calcium level by propranolol. The patient did not remember how long he had been taking the drug. However, when the drug was stopped, there was a rapid rise in the parathyroid hormone level (Fig. 7). But since parathyroid hormone secretion from neoplastic tissue is under the feedback inhibition of calcium,^{21,22} the use of calcitonin to lower the serum calcium may have contributed to this rise by removing the calcium induced inhibition. It does serve to emphasize that patients with primary hyperparathyroidism who refuse surgery and are either on propranolol for suppression of PTH or for hypertension, may have their symptoms suppressed, while their underlying process continues (in some cases masking a malignancy). Hypertension occurs in 50-70%^{23,24} of cases of primary hyperparathyroidism and within the hypertensive population, 1 in 130 has primary hyperparathyroidism.²⁵

An additional interesting feature of this case was the presence of two other apparently neoplastic lesions. The intracranial lesion was considered to be an inactive meningioma. The extracranial lesion was consistent with a lipoma or neurofibroma but was not biopsied. Without histological confirmation, questions concerning the possible diagnosis of MEN I, MEN III (IIb)²⁶ and von Recklinghausen's disease are unanswerable. Suffice it to say that lipomas have been associated with MEN I²⁶ and neurofibromas with MEN III (IIb).^{27,28,30} The patient did not have the pituitary or pancreatic lesions of MEN I and the multiple mucosal neuromas and marfanoid habitus of MEN III (IIb) were absent. Meningiomas and neurofibromas have both been considered part of von Recklinghausen's disease.²⁷ The neurofibromas of the latter disease have a predilection for the head, face, neck and trunk.²⁹ Precise diagnosis must await clinical developments and therapeutic indications.

Second neoplasias associated with parathyroid carcinoma seem to be rare. Only Dr. Cope's case with a coexisting squamous cell lung carcinoma can be documented here.¹⁹ In this case the patient had evidence by CT scan of an intracranial calcified lesion thought to be meningioma and a lesion of the scalp of uncertain origin.

SUMMARY

A case of carcinoma of the parathyroid gland is reported and discussed. The clinical, surgical and pathological features of the tumor are presented and the approaches to therapy are discussed. Parathyroid carcinoma is the cause of a small percentage of the

cases of primary hyperparathyroidism. Characteristically, it is a low grade and hyperfunctioning malignancy. The diagnosis should be suspected in hypercalcemic patients with a very high serum calcium, a palpable neck mass, vocal cord paralysis, and in those patients where hypercalcemia recurs after parathyroid surgery. It may arise in the setting of familial hyperparathyroidism but is as yet undocumented in von Recklinghausen's disease or MEN. Early detection and excision is felt to be the most important aspect of therapy. Excision of hyperfunctioning metastases and medical management of hypercalcemia are the accepted means of treating recurrences and extensive disease. The possible role of propranolol in masking this diagnosis is uncertain. The use of this drug in treating recurrent disease is worthy of further consideration and study.

ADDENDUM

Follow-up in early April revealed the patient's serum calcium level to be normal. Recurrent hypertension was easily controlled without propranolol. The CNS lesion is unchanged on repeat CT scan.

ACKNOWLEDGEMENT

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New Health Practitioners in Maine:

An Assessment of Their Current Role

HENRY B. PERRY, M.D., PH.D. AND ELINOR L. REDMOND, B.A.*

One of the most important developments in the practice of medicine in the United States during the past decade has been the utilization of midlevel health professionals in roles which involve diagnosis and treatment of medical problems under physician supervision. Since the establishment of the first physician assistant program at Duke University in 1965, there have been an estimated 10,000 physician assistants trained. An estimated 13,000 nurse practitioners have been trained during this same period as well.¹ This effectiveness in patient care and high level of acceptance by patients has been well documented.^{2,5} In fact, in a major recent review of the quality of patient care provided by new health practitioners Sox³ stated that "the major recent development in primary care may be the discovery that appropriately trained nonphysicians can do much of the physician's work with apparent safety and satisfaction." The purpose of this report is to describe the current role of new health practitioners in the provision of patient care in Maine.

The major rationale for the rapid growth and development of the new health practitioner movement, encouraged by federal support for training programs, was to improve the geographic and specialty maldistribution of health manpower in the United States.⁷ Maine's largely rurally based population and its relatively modest economic status make it particularly susceptible to these problems. Studies of the geographic distribution of physician manpower have emphasized the importance of urbanization and median family income upon the physician's choice of location.⁸ Rushing,⁹ for instance, found in a national analysis that the number of physicians per capita at the county level correlated .45 and .38 with the levels of urbanization and median family income, respectively. Since 70% of Maine's population is widely dispersed outside of Standard Metropolitan Statistical Areas¹⁰ and its statewide median per capita income ranks thirty-seventh out of the fifty states,¹¹ one would expect to find physician manpower shortages in rural areas.

Although Maine's overall average of 1.39 physicians per 1000 population approximates the national average of 1.37,^{12,13} Table 1 demonstrates that, at the county level, Maine's physician manpower distribution is uneven relative to the population. Within each

county as well there is certainly a concentration of medical manpower in the largest communities. Since Maine counties cover rather large areas, this means that access to medical services in rural areas of Maine may be less than optimal.

In an analysis of the availability of primary care manpower in Maine, True, Caven and Frechette⁴ found that in 1976 the overall supply of primary care manpower for the state was 4.09 physicians per 10,000 population. As might be expected, these authors found a shortage of primary care manpower in rural areas, where the number of primary care physicians per 10,000 population was only 3.45.* Although there has been a net increase in the number of primary care physicians in Maine of 21% between 1976 and 1978, this has been largely in communities of 20,000 and over.¹⁵

Maine has recognized the potential contribution of new health practitioners in improving access to medical services throughout the state. Legislation and regulations formulated by the Maine Board of Registration in Medicine¹⁷ and Board of Nursing¹⁸ have authorized the role of physician assistants and nurse practitioners in the provision of patient care. Since 1972 the University of Southern Maine and the Maine Medical Center in Portland have collaborated in the training of family nurse associates (FNAs), who receive a certificate following the completion of an 18-month part-time (equivalent to 12 months full-time) course in the provision of primary care. Within the past year, the Maine Medical Center has also established a nine-month postgraduate "residency" program for 6 physician assistants annually to obtain special training in the provision of emergency medical services. It is anticipated that the graduates of this program will staff emergency rooms in hospitals in small communities which are unable to obtain the services of full-time emergency room physicians.

METHODS

During the summer and fall of 1979, nurse practitioners and physician assistants in Maine were surveyed by mailed questionnaire. Of the 116 Maine nurse practitioners surveyed, usable responses were received from 92, representing a response rate of 79%. Of the 92 nurse practitioners participating in the study, only 61 were found to be currently working as nurse practitioners. Our findings for nurse practitioners are limited to this group of 61. Usable

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This project was conducted while Dr. Perry was a surgical resident at the Togus Veterans Administration Hospital, and supported by grant HS03014 from the National Center in Health Services Research (DHEW) and #1507RR0580501 from the NIH.

*The U.S. Department of Health (formerly HEW) defines a health manpower shortage area as one in which the number of primary care physicians is less than 3.50 per 10,000 population.¹⁶

TABLE 1

DISTRIBUTION OF MAINE PHYSICIANS BY DEGREE OF URBANIZATION ^a					
Demographic County Classification	Number of Maine Residents	Percentage of Maine Residents	Number of Maine Physicians	Percentage of Maine Physicians	Number of MD's per 1,000 Population
Non-Metropolitan Counties With Fewer Than 25,000 Inhabitants	96,400	8.7%	75	4.9%	0.78
Non-Metropolitan Counties With 25,000 to 49,999 Inhabitants	204,100	18.5%	207	13.6%	1.01
Non-Metropolitan Counties With Over 50,000 Inhabitants	332,200	30.1%	415	27.3%	1.25
Counties Considered Potential SMSA's	139,300	12.6%	216	14.2%	1.55
Counties in SMSA's With Over 50,000 Inhabitants	333,000	30.1%	606	39.9%	1.82
Total	1,105,000	100.0%	1519	99.9%	

^aSource: Bureau of Health Planning and Development, State of Maine, 1979

responses were also obtained from 54 of 57 physician assistants currently employed in Maine, representing a response rate of 94%.

FINDINGS

Ninety-one percent of Maine nurse practitioners are women, in contrast to only seventeen percent of Maine physician assistants. Nurse practitioners are slightly older than physician assistants (median ages are 37.8 and 32.2 years, respectively). Nurse practitioners have been working in their role as a new health practitioner for a slightly longer period of time (44.1% of nurse practitioners and 35.3% of physician assistants completed their training prior to 1975).

Ninety-seven percent of the nurse practitioners attended certificate programs, with the remainder graduating from master's degree programs. Seventy-five percent of the active nurse practitioners attended the Family Nurse Associate Program sponsored jointly by the University of Southern Maine and the Maine Medical Center. One-third of these nurse practitioners had earned at least a baccalaureate degree prior to entering their nurse practitioner program, while the remaining two thirds had earned only an R.N. or associate degree.

Among the 32 nurse practitioner respondents who were not functioning as a nurse practitioner at the time of the survey, one-third (12) were working as a nurse, another third (11) were working outside nursing, and the remainder were unemployed (8) or obtaining further education (1). All of the physician assistant respondents were actively working as a physician assistant at the time of the survey. Maine physician assistants have attended 16 physician assistant training programs throughout the United States. The Dartmouth MEDEX program (now closed) has trained 24% of Maine physician assistants, and the Northeastern University Physician's Assistant Pro-

TABLE 2

SIZE OF COMMUNITIES IN WHICH MAINE NEW HEALTH PRACTITIONERS ARE LOCATED		
	Nurse Practitioners (n = 58)	Physician Assistants (n = 54)
0 - 5,000	51.7%	70.9%
5,000 - 10,000	12.1%	3.6%
10,000 - 25,000	15.5%	12.7%
25,000 - 50,000	6.9%	7.3%
over 50,000	13.8%	5.5%
	100.0	100.0

gram in Boston has graduated 17%.

The geographic location of Maine new health practitioners is shown in Tables 2 and 3. Over half of the nurse practitioners and physician assistants in Maine are working in towns and communities with 5,000 or fewer persons. The distribution of nurse practitioners by county population (shown in Table 3) is almost identical to that for primary care physicians, while physician assistants appear to be more heavily concentrated in more rural areas. Only 15% of physician assistants, in contrast to almost half of nurse practitioners, are located within an SMSA. Twelve percent of the nurse practitioners and 18% of the physician assistants are working in health manpower shortage areas identified by the federal government for Maine.

The employers of Maine new health practitioners are shown in Table 4. Supervising physicians in private practice and hospitals are the major employers for both groups. Nurse practitioners report an average of 2.0 different supervising physicians and physician assistants, 2.9. Three of the nurse practitioners, but none of the physician assistants, are supervised by osteopathic physicians. Table 5 demonstrates that supervising physicians are given quite high ratings by the respondents. The area of

TABLE 3

DISTRIBUTION OF PRIMARY CARE PHYSICIANS AND NEW HEALTH PRACTITIONERS IN MAINE BY COUNTY CLASSIFICATION*				
Demographic County Classification	Percentage of Maine Residents (n = 1,105,000)	Percentage of Maine Primary Care Physician** (n = 948)	Percentage of Nurse Practitioners (n = 58)	Percentage of Physician Assistants (n = 54)
Non-Metropolitan Counties With Fewer Than 25,000 Inhabitants	8.8%	7.6%	12.0%	10.9%
Non-Metropolitan Counties With 25,000 to 49,999 Inhabitants	18.5%	16.1%	12.1%	36.3%
Non-Metropolitan Counties With Over 50,000 Inhabitants	30.1%	25.8%	24.1%	18.2%
Counties Considered Potential SMSA's	12.6%	11.1%	5.2%	20.0%
Counties in SMSA's With Over 50,000 Inhabitants	30.0%	39.4%	46.6%	14.6%
	100.0%	100.0%	100.0%	100.0%

*Population and physician data provided by the Bureau of Health Planning and Development, State of Maine, Augusta.

**includes osteopathic and allopathic physicians

greatest dissatisfaction with supervision concerned the physician's efforts to improve the new health practitioner's clinical skills.

The practice settings of Maine new health practitioners are shown in Table 6. These data show the average percentage of time spent by each group in a given practice setting. The major practice setting was also determined for each respondent. The percentage distribution of respondents by major practice setting is virtually identical to that for the average amount of time spent in each setting. Respondents work in a wide variety of practice settings. Nurse practitioners report an average of 1.9 different practice settings in which each works, while physician assistants report 2.3. The leading practice setting for nurse practitioners is private solo or partnership practice, while for physician assistants it is the community-based clinic. Physician assistants, in contrast to nurse practitioners, spend a major portion of their time in emergency rooms, while nurse practitioners are more actively involved in the community health agencies and public schools. A similar percentage of nurse practitioners and physician assistants are working in remote or satellite clinics where a physician is not present a majority of the time (35.1% and 29.6%, respectively).

The major clinical activity of new health practitioners in Maine is shown in Table 7. Far and away the most frequent area of clinical activity for both groups is family practice. Seventy-two percent of the nurse practitioners and 81% of the physician assistants are working in primary care fields. Nurse practitioners are more frequently involved in pediatrics and internal medicine and its subspecialties while physician assistants are more frequently involved in

TABLE 4

EMPLOYERS OF NEW HEALTH PRACTITIONERS IN MAINE		
	Nurse Practitioners (n = 60)	Physician Assistants (n = 54)
Supervisory physician	31.7%	31.5%
Hospital	28.3%	31.5%
Community Organization	10.0%	11.1%
National Health Service Corps	5.0%	9.3%
Other organizations*	25.0%	16.6%
	100.0%	100.0%

*Among the "other" employers are (1) for nurse practitioners: a school of nursing, a nursing home, 2 college health services, a family planning association, a school district, and a family practice residency program, and (2) for physician assistants: a major industry, a regional health agency, a county jail, and a family practice residency program.

emergency medicine.

The extent of physician involvement in patient care provided by new health practitioners is described in Table 8 and is similar for both groups. Forty percent of the new health practitioners' patient encounters are provided without any specific physician input. In approximately one-third of the encounters, the patient is discussed with the supervising physician. In the remainder of the encounters, the patient is seen jointly by the new health practitioner and the supervising physician.

The allocation of time of new health practitioners among various professional activities is shown in Table 9 and found to be almost identical for the two groups. Eighty percent of their time is devoted to direct patient care activities, and half of this is during

TABLE 5

SATISFACTION WITH PHYSICIAN SUPERVISORS EXPRESSED BY NEW HEALTH PRACTITIONERS IN MAINE		
	Percentage Who Answered Yes	
	Nurse Practitioners (n = 58)	Physician Assistants (n = 54)
Does your supervising physician give your questions careful consideration?	95.0%	96.3%
Are you able to comfortably present problems, complaints, or suggestions to your supervising physician?	93.3%	92.6%
Does your supervising physician usually give you recognition for work well done?	89.3%	85.2%
Does your supervising physician take an interest in discussing problems in patient management with you?	87.9%	87.0%
Generally speaking, are you satisfied with the relationship you have with your supervising physician?	84.5%	90.7%
Do you feel that your ideas and suggestions are important to your supervising physician?	83.6%	96.3%
Does your supervising physician take a strong interest in you as a person as well as in how competently you do your job?	74.1%	75.9%
Does your supervising physician help you very much in improving your clinical skills?	59.6%	68.5%

periods when the supervising physician is absent from the practice setting.

The average number of ambulatory patient visits managed by new health practitioners in an average day is 16.4 for nurse practitioners and 16.5 for physician assistants. A comparison of the average work week is shown in Table 10. It is apparent that many nurse practitioners work part-time since the average work week for them is less than the normal work week. In fact, one-third of the nurse practitioners in our study work 20 hours per week or less. Physician assistants work considerably more hours during evenings and weekends than do nurse practitioners and they are on call more hours as well. Only 16% of the nurse practitioners are on call outside of regular work hours. Those that do take call are on call an average of 35.0 hours per person per week. Fifty-six percent of the physician assistants in Maine do take call, and are on call an average of 49.4 hours per person per week.

Among the new health practitioners currently working in Maine, there has been relatively little job turnover. The nurse practitioners have been employed in their current jobs an average of 4.6 years and physician assistants, 3.4 years. Each group has worked an average of 2.9 years per job, computed on the basis of their length of employment to date.

Table 11 describes those aspects of medical training in which new health practitioners feel inadequately prepared. Aspects of obstetrics and gynecology were mentioned more frequently than any other area by both groups. Psychiatry/counseling and orthopedics were also relatively commonly mentioned topics.

TABLE 6

PRACTICE SETTINGS OF NEW HEALTH PRACTITIONERS IN MAINE		
	Amount of Time Spent by the Average Practitioner in Specific Practice Settings	
	Nurse Practitioner (n = 61)	Physician Assistant (n = 54)
Private solo or partnership practice	23.5%	18.9%
Private group practice	6.3%	6.9%
Hospital emergency room	5.8%	21.7%
Hospital outpatient clinic	14.7%	9.9%
Hospital outpatient services	6.7%	6.6%
Community based clinic	14.3%	25.6%
Community health agency	8.9%	0.0%
Nursing home	2.2%	2.4%
Public school	3.7%	0.0%
Patients' homes	3.6%	2.4%
Other	10.3%	5.6%
	100.0%	100.0%

DISCUSSION

These findings demonstrate the important role which new health practitioners are playing in the provision of primary care medical services in Maine. It is surprising that True and his colleagues¹⁴ completely overlooked the current and potential role of new health practitioners in addressing the shortage of primary care manpower in Maine.

Although there has been a 19% increase in the overall number of physicians in Maine between 1976 and 1978, almost half (47%) of this increase has oc-

TABLE 7

MAJOR CLINICAL AREA OF ACTIVITY FOR NEW HEALTH PRACTITIONERS IN MAINE		
	Nurse Practitioners (n = 58)	Physician Assistants (n = 54)
Family/general medicine	44.9%	55.6%
General pediatrics	15.5%	3.7%
General internal medicine	12.1%	3.7%
Emergency medicine	0.0%	18.5%
Medical subspecialty	22.4%	3.7%
Surgery	3.4%	3.7%
Occupational medicine	0.0%	3.7%
Psychiatry/counseling	1.7%	0.0%
Other	0.0%	7.4%
	100.0%	100.0%

TABLE 8

EXTENT OF PHYSICIAN INVOLVEMENT IN SPECIFIC PATIENT ENCOUNTERS OF NEW HEALTH PRACTITIONERS IN MAINE		
	Average Percentage of Patient Encounters	
	Nurse Practitioners (n = 61)	Physician Assistants (n = 54)
Patient seen only by the new health practitioner and no consultation obtained	40.9%	40.7%
Patient seen only by the new health practitioner, but case discussed with the supervising physician	28.8%	35.2%
Patient seen together by the new health practitioner and the supervising physician	30.3%	24.1%
	100.0%	100.0%

curred in the three counties making up Maine's two SMSAs (Cumberland, Androscoggin, and Sagadahoc counties), where 30% of the population resides.¹⁵ Thus it appears likely that Maine's more rural areas will continue to need additional primary care manpower in order to facilitate access to medical services.

It is now becoming apparent that new graduates of family practice residency programs throughout the United States are locating primarily in smaller communities. In 1978, 40% of the initial 1,200 family practice graduates had settled in towns of fewer than 15,000 persons.¹⁹ In recognition of the marked trend toward partnership or group practice among young family practitioners, a population of 5,000 to 6,000 persons within a 10-15 mile radius would appear necessary in order to adequately support a partnership practice. Kane maintains that "communities that are too small to support the physician model or are too distant from larger communities for convenient travel will need to rely on nurse practitioners or physician's associates, with supervision from a group of physicians or health care institution".¹⁹ Such an

Continued on Page 213

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATIONS: For the prevention and treatment of nocturnal recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis, and static foot deformities.

CONTRAINDICATIONS: Because of the quinine content, Quinamm is contraindicated in women of childbearing potential, in pregnancy, in patients with known quinine sensitivity, and in patients with glucose-6-phosphate dehydrogenase deficiency. Hemolysis (with the potential for hemolytic anemia) has been associated with a G-6-PD deficiency in patients taking quinine.

PRECAUTIONS: Thrombocytopenic purpura may follow the administration of quinine in highly sensitive patients. Recovery will follow withdrawal of the medication.

Cinchona alkaloids, including quinine, have the potential to depress the hepatic enzyme system that synthesizes the vitamin K-dependent factors. The resulting hypoprothrombinemic effect may enhance the action of warfarin and other oral anticoagulants.

ADVERSE REACTIONS: Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. If ringing in the ears, deafness, skin rash, or visual disturbances occur, the drug should be discontinued.

DOSAGE AND ADMINISTRATION:

1 tablet upon retiring. When necessary, 1 additional tablet may be taken following the evening meal.

Product Information as of September, 1977

U.S. Patent 2,985,558

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TABLE 9

ALLOCATION OF PROFESSIONAL TIME FOR MAINE NEW HEALTH PRACTITIONERS		
	<i>Average Percentage of Time Spent in Activity</i>	
	<i>Nurse Practitioners (n = 61)</i>	<i>Physician Assistants (n = 54)</i>
Direct patient care with supervising physician present in the practice setting	40.4%	41.8%
Direct patient care with supervising physician absent from the practice setting	38.8%	41.0%
Administration	6.0%	5.0%
Teaching other health professionals	4.9%	4.0%
Clinical work	3.9%	3.0%
Technical or laboratory work	3.8%	3.0%
Other	2.2%	2.2%
	100.0%	100.0%

TABLE 10

AVERAGE WORK WEEKS OF NEW HEALTH PRACTITIONERS IN MAINE		
	<i>Nurse Practitioners (n = 61)</i>	<i>Physician Assistants (n = 54)</i>
Number of hours in regular work week (excluding hours on call)	32.1	45.5
Number of hours usually worked in evenings or during weekends in an average week	2.7	14.2
Number of hours on call outside of regular work hours	5.7	27.4

approach would appear to be feasible in Maine. Access to primary care services would be greatly improved by the expansion of the number of new health practitioners in rural areas.

Our data indicate that new health practitioners in Maine function relatively independently, although still under physician supervision. As the competency and experience of these individuals increase, they will likely become even more functionally independent from their supervising physicians. As long as suitable referral and backup physician support is available, such independence would have the advantage of making services more readily available to dispersed population groups such as Maine has.

A rather marked difference was observed between nurse practitioners and physician assistants in their location in small communities and more rural areas and also in the number of hours worked per week. Similar findings have been observed in large scale studies of these two groups as well. Nationwide, 40% of physician assistants in comparison to 24% of nurse practitioners are working outside of SMSAs.²⁰ Even within the physician assistant profession, women are less likely than men to choose rural areas of employment.²¹ Nationally, physician assistants ap-

TABLE 11

AREAS IN WHICH NEW HEALTH PRACTITIONERS IN MAINE EXPRESSED A DESIRE FOR MORE TRAINING		
	<i>Percentage of Respondents Desiring More Training</i>	
	<i>Nurse Practitioners (n = 61)</i>	<i>Physician Assistants (n = 54)</i>
Obstetrics & Gynecology (pre- and postnatal care, family planning, office gynecology)	16%	30%
Psychiatry/counseling (psychiatric emergencies, sexual dysfunction, behavior problems in childhood and adolescence, stress reduction and conflict management)	15%	15%
Orthopedics (radiological diagnosis of fractures, casting, sports medicine, treatment of musculoskeletal problems)	11%	20%
Legal-Administrative Matters (malpractice prevention, office management skills, personnel management)	11%	13%
Pharmacology (indications, actions, dosages, and side effects of commonly used drugs)	8%	9%
Office Laboratory Techniques (performance and interpretation of common laboratory tests)	10%	4%
Pediatrics (normal growth and development, diagnosis and management of common minor illnesses)	11%	7%
Other Specific Skills (neurological exams, ophthalmo- logic and ENT exams, management of diabetes, suturing of minor wounds, radiological interpretation)	11%	13%

pear to provide about 8 more hours per week of direct patient care than do nurse practitioners.²²

Study respondents appeared eager for opportunities to continue to upgrade their skills and knowledge in areas relevant to their practices. The development of short postgraduate courses and programs geared to these needs would be a valuable contribution toward maintaining the clinical skills of new health practitioners in Maine.

Although the major contribution of the new health practitioners movement in Maine, as in the United States, has been in the provision of primary medical care services, there is increasing interest in the role of these health professionals as "surrogate house officers" in non-primary care fields, both in hospitals which have housestaff with work loads beyond their capacity or in community hospitals without housestaff which desire housestaff type manpower. During the next decade we can expect increasing numbers of new health practitioners in Maine in these roles, particularly in surgical specialties and medical subspecialties.

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LEGIONNAIRES' DISEASE: Recognition of the Togus Strain—Continued from Page 202

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Gastric Devascularization with Preservation of the Left Gastric Artery for Control of Massive Hemorrhage

FENNELL P. TURNER, M.D.*

Surgical measures for the control of bleeding from acute hemorrhagic gastritis have included suture ligation of multiple bleeding sites, vagotomy with drainage, distal partial gastrectomy (Madlener procedure) and high sub-total gastrectomy. Failure to control bleeding has been common with all of these measures and near total or total gastrectomy has sometimes been required.

Several years ago an alternative procedure for control of gastric hemorrhage was proposed by Rittenhouse, McFee and Aust.¹ This consisted in a "four-point gastric vessel ligation." The right and left gastric arteries were ligated along the lesser curvature usually through a lesser sac approach and the right and left gastro-epiploic arteries were ligated at their origins on the greater curvature. "The short gastric arteries, the splenic artery, the esophageal branch of the left gastric artery and the gastroduodenal arteries were avoided when possible." In a subsequent paper,² twenty-one cases were reported with immediate cessation of bleeding in all twenty-one patients. Five patients had had prior gastric surgery. Recurrent bleeding occurred in two patients (9%). All patients were said to be critically ill and the mortality was high (38%). Two of the eight patients reported by Rittenhouse, et al, had splenectomies and there was history of previous splenectomy in three of the twenty-one patients reported by Richardson and Aust with incidental splenectomy in a fourth patient at the time of devascularization.

In this presentation, I would like to describe two clinical histories where, in order to control continuing hemorrhage, gastric devascularization was carried out with preservation of the left gastric artery, rather than with preservation of the short gastric vessels. In these two patients, ligation and division of all vessels along the greater curvature, including all of the vasa brevia, was purposefully carried out.

CASE REPORTS

Case 1. On April 14, 1971, exploratory laparotomy, gastrotomy, vagotomy and pyloroplasty were performed on a 44-year-old male with diffuse gastric hemorrhage. This patient had been in the habit of taking up to 60 grains of aspirin daily for the relief of arthralgia. In addition, for several days prior to admission, because of rhinorrhea, he had been dosing himself with an unknown quantity of nose drops and cold tablets. His initial hemoglobin was 5.4 and Hematocrit was 16%. During the first 24 hours in the hospital, intensive medical management was carried out. During this period of time, 5 blood transfusions were required. As severe bleeding con-

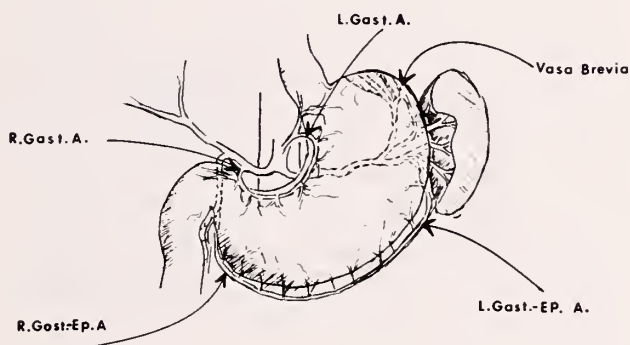


Fig. 1 Major Arteries of Stomach

tinued, exploratory laparotomy and gastrotomy was performed. This failed to reveal a bleeding source. A vagotomy and pyloroplasty was then carried out. Following operation, as bleeding continued, esophagogastroscope was performed. Several punctate bleeding areas were poorly seen on either side of the esophagogastric junction. Celiac angiography was also carried out with failure to clearly reveal the source of bleeding. Repeat gastroscopy was then done 8 days after the first operation, and this time active bleeding was visualized from multiple punctate bleeding sites in the gastric cardia and upper fundus. A second operation was carried out on April 22, 1971. Many tiny ulcers, from 1 to 3 mm in diameter, were found on the greater curvature and posterior wall of the fundus and cardia near the esophagocardiac junction. Arterial bleeding from some of these areas was clearly seen. Several unsuccessful attempts were made to undertake suture ligation of these bleeding areas. It was then decided to devascularize the area rather than carry out a total or near total gastrectomy. Accordingly, all vessels along the greater curvature including all the vasa brevia were divided and ligated. The spleen was removed as it was strongly adherent to the stomach. This decision was easily made as a large well-vascularized accessory spleen 6 or 7 cm in diameter had been found in the gastrocolic omentum. A 60% partial distal gastrectomy with Billroth I anastomosis was also performed. Following this gastric devascularization, with preservation of the left gastric artery, the color of the proximal gastric pouch seemed normal. All bleeding from the multiple small ulcers in the fundus and gastric cardia had immediately ceased following ligation of the short gastric arteries.

Histological study of the resected distal stomach also revealed evidence of a well-healed lesser curvature gastric ulcer. Post-operative convalescence was uncomplicated during this 8-day acute illness including two operative procedures. Nineteen blood transfusions had been administered.

Case 2. This patient was a 70-year-old male who gave a story of having been drinking heavily prior to admission to a small local hospital for severe gastrointestinal bleeding. Thirty-six hours later during which time he had received a total of 11 blood transfusions, he was transferred to VA Medical Center, Togus, Maine on April 27, 1977. On admission to the community hospital, his hemoglobin had been found to be 6.5 and Hematocrit 21, and at the time of transfer to VA Hospital, Togus, Maine his Hematocrit had risen to 27.

Esophagogastroscope was carried out and this revealed large amounts of clotted blood without clear evidence of active bleed-

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ing. Accordingly, conservative therapy was again instituted and over a period of the next 24 hours his circulatory status was maintained by an additional 5 units of blood. At the end of this period, his Hematocrit had now fallen to 24. Emergency partial gastrectomy, with antecolic Hofmeister Billroth II anastomosis and tube duodenostomy was carried out on April 28, 1977. An actively bleeding posterior wall duodenal ulcer was found. The ulcer was partly removed and the bleeding site was suture ligated. A chronic gastric ulcer 1 cm in diameter was also found on the lesser curvature of the resected stomach. Within a short time after the return of the patient to the ICU, severe gastric bleeding re-occurred. Once again conservative management (gastric lavage with iced saline and vasopressors intravenously) was unsuccessful, and re-operation was carried out on April 29, 1977. At this time, the patient was found to have diffuse bleeding from cardia and posterior wall of the fundus and body of the stomach where there was gross evidence of acute hemorrhagic gastritis. Following the gastrotomy, a vagotomy and ligation and division of all remaining vessels along the greater curvature, including all of the short gastric vessels was carried out, the spleen being left in situ. Gastric bleeding thereupon immediately ceased. The postoperative course was stormy and the patient required intensive care for postoperative respiratory failure, pneumonitis and gastrocutaneous fistula. Recovery, however, was complete and eventually the patient was discharged from the hospital on July 7, 1977. This patient had also received 19 bottles of whole blood during the course of his illness.

SUMMARY

Two cases have been presented where massive gastric hemorrhage from acute hemorrhagic gastritis in the proximal stomach was controlled by means of gastric devascularization including division of all vasa brevia, but with preservation of the left gastric artery. This operative approach, in contrast with the procedure advocated by Rittenhouse, et al, may be the treatment of choice in instances where severe gastric hemorrhage has occurred from multiple areas of "stress" ulceration or from areas of acute erosive gastritis in the fundus and upper body of the stomach, as well as on the greater curvature of the gastric cardia.

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GROUP NUMBER XYZ111	BLUE SHIELD PLAN CODE 222	BLUE CROSS PLAN CODE 111
GROUP NAME XYZ CORPORATION		

Subscriber's Name —

Group Number —

Subscriber's Identification Number —

Be sure to give your local Blue Cross and Blue Shield Plan these three pieces of information!

What is "Central Certification?"

"Central certification" is a special way of covering certain Blue Cross and Blue Shield Plan subscribers. It is used for employees of a company that has plants, offices and people in several different states; whose employees often travel a great deal or change location frequently; and which has all of its personnel, payroll and health coverage records in one place.

For these companies, Blue Cross and Blue Shield Plans offer central certification.

All records are kept by one Plan, (called the "control Plan"), which is usually the Plan located in the company's headquarters city.

The control Plan issues identification cards to all employees of that company, regardless of their location.

However, a central certification subscriber is treated exactly like any subscriber of your local Blue Cross and Blue Shield Plan. You accept the central certification card just as you accept a card from your local area Plan.

The Card

The card—a sample is reproduced at the top of this guide—is distinctive. It is carried only by central certification subscribers. Along with the subscriber's name and identification number, the card also has a six-character group number that is special. The three letters identify the company the subscriber works for and the three numbers identify the Blue Cross and Blue Shield control Plan.



What You Do

When a central certification subscriber comes to you for care, treat the patient exactly as you would any other Blue Cross and Blue Shield Plan subscriber. Give your local Plan:

the name: John Q. Public
the identification number: XYZ123456789
the group number: XYZ111

The local Plan will then cover the benefits to which that subscriber is entitled.

Special Note: Report both outpatient cases and inpatient cases to your local Blue Cross and Blue Shield Plan. Most central certification subscribers have comprehensive coverage, including outpatient benefits.

After the patient is discharged, or has received outpatient services, the local Blue Cross and Blue Shield Plan will pay you just as it would for any of its local subscribers.

Please Remember . . .

Central certification is a great convenience for a company with employees scattered throughout several states.

In almost all cases, the patient lives and works in your community.

Just remember that the central certification subscriber—as far as you're concerned—is exactly the same as any local Blue Cross and Blue Shield Plan subscriber.

You deal only with your local Blue Cross and Blue Shield Plan.

You will be paid by the local Blue Cross and Blue Shield Plan.

Diagnostic Imperatives In Internal Medicine

The Timely Detection of Treatable Disease

Hematology

JANE F. DESFORGES, M.D.*

In hematology there are situations where early diagnosis can avert distress and disability and, in the most extreme cases, where it can prevent mortality by starting proper treatment. Diagnosis of hematologic disease follows two basic principles. First, one should determine whether the specific manifestation reflects a basic hematologic abnormality or is secondary to another underlying systemic disease. Second, one must determine the kinetics involved, that is whether there is a defect in production, either quantitative or qualitative, or whether there is an increased rate of loss of the involved molecule or cellular element.

THE BLEEDING PATIENT

Historical Clues

It is often possible to characterize the mechanism of bleeding by eliciting a few salient historical points. If the patient has a chronic history of bleeding tendency, a *family history* may be helpful in confirming the congenital nature of the abnormality and also to some extent in delineating which abnormality may be present. A family history implying sex-linked inheritance suggests deficiency of factor VIII or IX. Other familial bleeding disorders are autosomal in nature, with a pattern of dominant inheritance suggesting von Willebrand's disease, one of the more common inherited bleeding disorders, or certain inherited platelet defects. On the other hand, bleeding related to factor XI deficiency or factor XIII deficiency might be considered if the history is that of an autosomal recessive trait.

Other clues may be in the *patient's environment*. In any patient, aspirin, if not a cause of hemorrhagic tendency can exacerbate a latent disorder. Anticoagulant medication should always be considered. Aside from the effects of coumadin drugs, vitamin K deficiency can also occur in patients who have received only parenteral feedings and have been treated with antibiotics for prolonged periods. The patient receiving quinidine is at risk for quinidine-induced thrombocytopenic purpura. Drugs such as procainamide or isoniazid may induce a circulating anticoagulant. In the bleeding patient all medications should be carefully reviewed. Recent infections must always be suspected as causes of thrombocytopenia; a very mild case of rubella, for example, may be followed by a very severe case of thrombocytopenia.

Clues on Physical Examination

If the patient has a *petechial eruption* with or

TABLE I

CLINICAL CLUES TO NATURE OF BLEEDING DISORDER	
FEATURE	SUGGESTS
Family History of Bleeding:	
Sex-Linked	VIII or IX Deficiency
Autosomal Dominant	Von Willebrand's Disease; certain platelet defects
Autosomal Recessive	XI or XIII Deficiency
Exposure to Certain Drugs	Platelet or Coagulation Abnormalities
Petechiae	Platelet or Vascular Abnormalities
Spontaneous Ecchymoses or Hematomas	Coagulation Defects

without ecchymoses, quantitative and qualitative abnormalities in platelets or abnormalities in the vascular wall should be considered the likely defects. If the patient has multiple *ecchymoses without petechiae*, coagulation abnormalities are a more likely mechanism, especially if the bruises are truly spontaneous. In patients with single hematomas such as may occur in muscles, in the retroperitoneal area, or in the joint spaces, an abnormality of coagulation is almost always the mechanism involved; hemarthrosis makes deficiency of factor VIII or IX most likely. Bleeding into areas of pressure ("saddle ecchymoses") in patients with a history of dietary deficiency should suggest scurvy. If there is a purpuric rash associated with other dermatologic manifestations, arthritis, or abdominal signs, one should be alert to the possibility of vasculitis.

Laboratory Findings

Tests needed to evaluate the mechanism of bleeding are few. Careful *observation of the blood smear* will demonstrate whether the platelets are adequate in number and also will allow a quick estimate of whether there are any associated abnormalities of the white cells as one might see in disease of the marrow. *Platelet count* and *bleeding time* provide adequate assessment of quantity and function of platelets. If both are abnormal, then one must determine the mechanism of thrombocytopenia to pursue proper treatment. This requires study of bone marrow to assess the rate of platelet production. If only the bleeding time is abnormal, special studies of platelet function are necessary to delineate the defect. If both findings are normal in a patient with a petechial eruption, a vascular defect, usually vasculitis, is the probable cause.

*Division of Hematology-Oncology, New England Medical Center Hospital, Boston, Massachusetts.

TABLE 2

TESTS USEFUL IN DIAGNOSIS OF BLEEDING DISORDERS	
TEST	USEFUL IN DIAGNOSIS OF
Blood Smear	Platelet abnormalities; associated abnormalities of WBC or RBC
Platelet Count	Thrombocytopenia; Thrombocythemia
Bleeding Time	Qualitative or Quantitative abnormality of platelets; von Willebrand's disease
Thrombin Time	Presence of heparin; Disseminated Intravascular Coagulation; Congenital abnormalities of fibrinogen
Prothrombin Time	Vitamin K deficiency; Liver disease
Partial Thromboplastin Time	Abnormality of Factors VIII, IX, XI; Circulating anticoagulant; von Willebrand's disease

A rare cause of bleeding is an overabundance of platelets. *Thrombocythemia*, a proliferative disease in which the platelet count may be two million or more, can be associated either with thrombosis or with hemorrhage. Platelet function in this disease is abnormal but appears to improve as the platelet count is brought below a million. In situations where there are complications of bleeding or thrombosis, treatment should be immediate and is carried out by *plateletpheresis*. More chronic management of the disease is achieved by the use of myelotoxic drugs such as *busulfan*.

To assess coagulation abnormalities, three screening tests should be carried out. They are the *thrombin time*, *prothrombin time* (PT) and the *partial thromboplastin time* (PTT). Prolongation of the thrombin time reflects the presence of split fibrin products released in Disseminated Intravascular Coagulation (DIC) and is a major factor in causing bleeding in that syndrome; a prolonged thrombin time may also be due to the presence of heparin, or to severe abnormalities in fibrinogen.

A prolonged prothrombin time may reflect vitamin K deficiency and requires a search for the mechanism as well as the institution of replacement therapy. In most cases, however, a prolonged PT is secondary to liver disease.

The PTT is prolonged in deficiencies of factor VIII, factor IX and factor XI as well as in those states with a circulating anticoagulant. von Willebrand's disease is one state where there is a coagulation defect manifest by a prolonged PTT as well as a hemostatic defect manifest by a long bleeding time. If the PTT is prolonged, more precise tests are necessary to determine the specific deficiency or the area of action of the inhibitor to clotting in order to select proper treatment.

Treatment

The treatment of bleeding disorders depends on their cause. If the abnormality is related to thrombocytopenia, platelet kinetics determine the next step. If there appears to be increased destruction, *prednisone* therapy may provide fairly rapid hemostasis. *Platelet transfusion* should be used only

TABLE 3

EVALUATION OF ANEMIA	
CHARACTERISTICS OF ANEMIA	LOOK FOR
Normocytic, Normochromic	Inflammation, cancer, renal failure, endocrine failure
Hypochromic microcytic	Cause of blood loss
Macrocytic	Nutritional cause of folic acid deficiency; Evidence of combined system disease suggesting B ₁₂ deficiency
With increased reticulocyte count	Evidence of hemolysis

when bleeding is in critical sites since the survival of these elements is very short and the effect very transient in this setting. When the defect is one of production, however, platelet transfusions are effective in controlling active bleeding. This treatment should still be reserved for serious hemorrhage since these patients will eventually become immunized to the transfused platelets thus diminishing their effect.

For patients with abnormalities of coagulation several forms of therapy exist. For those individuals with factor VIII deficiency, classical hemophilia, *factor VIII concentrates* are available. For patients with factor IX deficiency, Christmas disease, *preparation of factor IX* can be used. In von Willebrand's disease, either *cryoprecipitate* or *frozen fresh plasma* is effective. For other deficiencies, the best source is *frozen fresh plasma*. Schedules vary depending on the deficiency. If an anticoagulant is present, however, enormous amounts of the inhibited factor may be needed. In all cases, frequent assays of the specific clotting factor should be made during treatment.

THE ANEMIC PATIENT

Anemia—A Secondary Disorder

Anemia is most often *secondary to another underlying disease*. The onus is on the physician, therefore, to look for the cause. The usual anemia in chronic disease, be the disorder infectious, inflammatory or metabolic, is normocytic and normochromic—a very non-specific finding. If, instead, hypochromic microcytic anemia is noted, this is an extremely important signal because it may reflect occult blood loss and may be the only manifestation of a disease which requires early attention to avoid fatality. In such a patient, therefore, one should pursue further documentation of iron deficiency, usually easily done with measurement of serum iron and iron binding capacity, and search for the source of bleeding. Even where there is a history of known bleeding such as menorrhagia, it is wise to check the gastrointestinal tract in order to avoid possibly missing occult malignancy. One should proceed with upper and lower gastrointestinal studies by x-ray as well as sigmoidoscopy unless repeated tests for occult blood in the stool are negative and another cause is well documented. Of all the patients seen with iron

deficiency, the number with occult cancer in the gastrointestinal tract will be low, but the payoff in finding such cases is extremely high and therefore the search is justified.

Anemia—A Primary Disorder

Megaloblastic states. There are other types of anemia where the basic disease is hematologic. Of all of these, the one which demands immediate attention is the macrocytic anemia which may be due to B₁₂ deficiency. Since this has a high morbidity, its documentation should be aggressively pursued. The presence of *macrocytic indices* together with *hypersegmented polymorphonuclear leukocytes* in the peripheral blood is adequate evidence of megaloblastic anemia. One must then determine whether the patient has *folate or B₁₂ deficiency*. Evidence for the former is often elicited by looking for an underlying disease leading to malnutrition, malabsorption or a physiologic or pathologic state with increased demand for the vitamin. Examples include alcoholism or pregnancy; a low concentration of serum folate confirms the diagnosis. With B₁₂ deficiency, usually due to pernicious anemia, there may be neurologic involvement of the posterior or lateral columns which should alert one to this diagnosis. Occasionally cerebral manifestations may dominate the neurological picture ("megaloblastic madness"). Measuring serum B₁₂ concentration is useful although technical problems in the measurement may make the diagnosis based on this alone uncertain. When one is in doubt, a therapeutic trial of B₁₂ should be given before folic acid is used. Inappropriate use of folic acid in a B₁₂ deficient patient could induce a temporary hematologic response to folic acid while neurologic deficits progress.

Hemolytic states. Evidence of hemolysis can be simply assessed by evaluating the rate of production, i.e., the reticulocyte count necessary to maintain a given hematocrit over a period of days. There may not always be time, however, to carry out such prolonged observations and one may have to be satisfied with the finding of anemia associated with an elevated reticulocyte response in the absence of blood loss.

To focus on the mechanism of hemolysis, history, physical findings and observations of the blood smear are all helpful. Besides *past history* of anemia in the patient, a *family history* of jaundice, gallstones, splenectomy or anemia points to congenital hemolytic anemia and therefore an intrinsic red cell defect. A history of recent or sudden onset of the disease on the other hand, points to an acquired disorder and demands careful inquiry regarding drug exposures, or recent illnesses, such as mycoplasma infection. In persons of African or Mediterranean descent, deficiency of the enzyme, glucose-6-PO₄ dehydrogenase, can result in brisk hemolysis on exposure to certain drugs, e.g., primaquine, some sulfa drugs, nitrofurantoin or even febrile illness. *Splenomegaly* suggests those hemolytic states which

Continued on Page 221

Tenuate®

(diethylpropion hydrochloride NF)

Tenuate Dospan®

(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect, rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle, the patient should therefore be cautioned accordingly. **Drug Dependence:** Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychological dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. **Use in Pregnancy:** Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. **Use in Children:** Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: **Cardiovascular:** Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. **Central Nervous System:** Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache, rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. **Gastrointestinal:** Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. **Allergic:** Urticaria, rash, ecchymosis, erythema. **Endocrine:** Impotence, changes in libido, gynecomastia, menstrual upset. **Hematopoietic System:** Bone marrow depression, agranulocytosis, leukopenia. **Miscellaneous:** A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSEAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride) One 25 mg tablet three times daily, one hour before meals, and in mid-evening, if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release. One 75 mg tablet daily, swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSSAGE: Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.
Cayey, Puerto Rico 00633

Direct Medical Inquiries to
MERRELL-NATIONAL LABORATORIES
Division of Richardson-Merrell Inc.
Cincinnati, Ohio 45215, U.S.A.

Licensors of Merrell®

References: 1. Citations available on request from Medical Research Department, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga, M.T., O'Dillon (Dillon), R.H., and Leyland, H.M. A comprehensive review of diethylpropion hydrochloride. In: *Central Mechanisms of Anorectic Drugs*, S. Garattini and R. Samanin, Ed. New York: Raven Press, 1978, pp 391-404.

Merrell

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TABLE 4

USEFUL LABORATORY TESTS IN EVALUATING HEMOLYSIS		
	USEFUL IN:	EXAMPLES
Routine Blood Smear	States with abnormalities of RBC	Sickle cell anemia, Microangiopathic hemolytic anemia
Supravital Stain	Heinz body formation	Drug induced hemolytic anemia
Hemoglobin electrophoresis	Hemoglobinopathies	Thalassemia, sickle cell anemia
Osmotic Fragility	Spherocytes	Congenital spherocytosis
Coomb's Test	States with IgG coating red cells	Autoimmune disease, certain transfusion reactions
Cold Agglutinin Titer	States with abnormal cold agglutinins	Autoimmune disease

depend on splenic trapping and extravascular hemolysis, whether mechanical as in spherocytosis or immunologic as in autoimmune disease associated with an IgG antibody.

Observation of the *blood smear* is always informative. The picture may be as obvious as sickle cell anemia with the presence of irreversibly sickled cells or as subtle as drug-induced hemolytic anemia where special staining is required to demonstrate Heinz bodies. The answer, is however, often there for the looking. *Confirmatory tests* such as hemoglobin electrophoresis when hemoglobinopathy is suspected, G6PD assay in drug-induced hemolysis, osmotic fragility in spherocytosis or urine hemosiderin in microangiopathic states are indicated when further clarification is necessary. If examination of the smear does not suggest the underlying hemolytic disease, one should consider those syndromes without abnormalities in red cell morphology—especially autoimmune disease. A Coombs test and cold agglutinin titer could be the next step.

Treatment of hemolytic anemia depends on the mechanism of hemolysis. In spherocytosis, for example, splenectomy eliminates the trap and cures the hemolytic state: in IgG autoimmune disease, prednisone controls the disease, but splenectomy may be necessary as well. However, splenectomy is unlikely to improve hemolytic anemia due to cold agglutinin, nor is it the treatment in sickle cell anemia where autosplenectomy occurs *pari passu*. In some cases, elimination of an agent is the appropriate treatment. This may mean, for example, withdrawal of an offending drug causing Heinz body anemia, or, perhaps, repair of a leaking prosthetic heart valve which is destroying red cells intravascularly because of turbulent blood flow.

In patients known to have a chronic hemolytic state, one must always be alert to the sudden development of further anemia. This may reflect an *aplastic crisis*, in which the marrow abruptly ceases erythropoiesis for a short period of time. Because of short red cell survival, profound and even fatal

anemia may occur within a few days if the patients are not transfused. Such crises may occur spontaneously or be associated with viral illness. Monitoring the reticulocyte count will alert the physician to the necessity for transfusions until marrow recovery occurs.

ABNORMALITIES OF WHITE CELLS

If in the course of examining an asymptomatic patient, leukocytosis or leukopenia is noted there is the dilemma of how far to pursue the finding. If the patient has an absolute lymphocytosis and is without other signs, the likely diagnosis is chronic lymphocytic leukemia and in such a setting there is rarely need to pursue the diagnosis further since no treatment is indicated. If there is *granulocytosis*, with or without a left shift, again in a patient free of symptoms, one can carry out some simple tests to differentiate leukemoid reaction from myelocytic leukemia. The distinction is important not simply to document the presence of leukemia but rather to determine whether there is a leukemoid reaction reflecting an unrecognized disease. There are two helpful points. First, basophils are not seen in the leukemoid reaction but are usually seen in myeloproliferative disease. Second, the leukocyte alkaline phosphatase is elevated in a leukemoid reaction and depressed in chronic myelocytic leukemia. If leukemoid reaction is suspected then one should consider searching for infection or occult malignancy. Prime suspects are cancer of the lung or the kidney.

The opposite finding, *neutropenia*, in an apparently healthy subject is more of a dilemma. It is worth remembering that black people may normally have WBC as low as 4000. Careful history should elicit possible exposure to any chemical or medication which might induce neutropenia. Such should, of course, be withdrawn. If there is no evidence of toxic exposure, and no underlying disease, such as infection or lupus erythematosus, it is extremely unlikely that further testing would change the immediate management of the patient. Because of this, the best approach in general is simply to reevaluate at intervals to determine whether this finding is the harbinger of disease which may later be clinically important.

With *agranulocytosis*, the clinical picture is usually dramatic and the cause usually apparent. Typically, patients with this condition have high fever and severe oral or pharyngeal ulceration. The syndrome, when due to drugs, may develop abruptly even after weeks or months. Treatment should be prompt and intensive. All possibly offending medication should be omitted. The patient should be admitted to the hospital, treated with antibiotics after blood cultures have been drawn and kept in isolation; if possible white cell transfusions should be provided.

THE PATIENT WITH MARROW FAILURE

When patients have evidence of more than one cell line depressed, the problem is usually in the marrow

TABLE 5

CLINICAL SYNDROMES ASSOCIATED WITH TOO MANY BLOOD CELLS

ENTITY	SYNDROME
Polycythemia vera	Neurologic abnormalities, Peripheral ischemia
Thrombocythemia	Peripheral ischemia
Chronic myelocytic leukemia with extremely high WBC	Neurologic abnormalities rare
Acute leukemia with WBC >100,000	Cerebral hemorrhage

itself. The peripheral blood, however, may give clues to the nature of the underlying disease. Thus, if no abnormal cells are seen in the peripheral blood smear, the most likely disease is aplastic anemia. Accurate diagnosis of this disease should involve bone marrow biopsy because an aspirate alone may be insufficient to assess cellularity. In contrast, if abnormal cells are seen in the peripheral blood, marrow examination is likely to show infiltration either by leukemic cells, which may be evident in the peripheral blood, or by metastatic carcinoma in patients who have a leukoerythroblastic blood picture.

In all these patients, it is urgent to know the basic cause in order to plan treatment. Immediate therapy involves replacing the formed elements as necessary. Long term plans may include marrow transplantation for aplastic anemia or chemotherapy in the patient with acute leukemia, aiming at long-term remission or cure.

THE PATIENT WITH TOO MANY BLOOD CELLS

Myeloproliferation

Patients may have symptoms of *vascular insufficiency* as their first manifestation of a myeloproliferative syndrome. In polycythemia vera, the viscosity associated with high hematocrit may result in neurologic syndromes ranging from headache to visual disturbance to stroke. When thrombocythemia is the major abnormality, the microvasculature may be involved—sometimes leading to painful ischemic toes or feet in the presence of good pulses. Extremely high white counts in chronic myelocytic leukemia may also be associated with cerebrovascular symptoms, but this is rare. In acute leukemia with high levels of circulating “blasts,” however, white cells do pose a threat to the cerebral circulation by infiltrating vessel walls.

Chronic myelocytic leukemia produces symptoms in several ways. As it progresses, normal erythropoiesis is depressed and *anemia* ensues. While *thrombocytosis* may occur early in the disease, later *thrombocytopenia* may be an added complication with its own side effects. *Splenomegaly* may lead to clinical symptoms and occasionally splenic infarction becomes a major problem. At the point where the disease is associated with symptoms, the diagnosis is apparent, being manifest both by leukocytosis with left shift, basophils, anemia and splenomegaly.

Treatment of myeloproliferative disorders depends on the clinical manifestation. In chronic myelocytic

TABLE 6

CAUSES OF ISOLATED ERYTHROCYTOSIS

Chronic Hypoxia
Lung Disease
Cyanotic heart disease
Erythropoietin—producing tumor
Hypernephroma
Hepatoma
Cerebellar hemangioblastoma
Congenital hemoglobinopathy (rare)
Idiopathic

leukemia, alkylating agents or hydroxyurea are used to eliminate the mass of leukemic cells. In polycythemia vera, phlebotomy is effective treatment to relieve quickly the manifestations of increased viscosity while plateletpheresis and cytotoxic drugs may be necessary to control platelet levels. Given moderately increased values for red cells, white cells, and/or platelets, without symptoms however, there is no indication to treat.

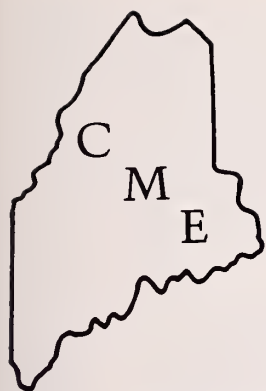
Erythrocytosis

There is reason to pursue the incidental findings of an elevated hematocrit without associated changes in white cells or platelets. Polycythemia vera is almost always associated with one or more abnormalities besides an elevated red count, such as leukocytosis, elevated leukocyte alkaline phosphatase, thrombocytosis or splenomegaly. If the red cell mass is truly increased, one should therefore pursue other causes with appropriate studies. This may simply require a physical examination to demonstrate chronic lung or heart disease with cyanosis. It may, however, demand careful study of liver, kidneys and central nervous system to rule out an erythropoietin producing tumor, such as hypernephroma. Rarely, its cause may be a congenital abnormality in hemoglobin. To miss the latter diagnosis is unimportant. To miss the renal tumor, however, may be fatal for the patient.

ADENOPATHY AND SPLENOMEGALY

Silent adenopathy should always be considered potentially serious. In patients who have, for example, a tender node draining infection, or adenopathy associated with an acute viral syndrome, the physician need not study it further. When this finding occurs without an explanation, however, diagnostic measures should be pursued. If there is diffuse adenopathy, there may also be pathologic findings in the bone marrow which can be documented by marrow biopsy, a technique more useful for demonstrating lymphoma than the traditional aspirate. The most reliable way of achieving a diagnosis, however, is biopsy of the node itself, and there should be no delay in doing this. If the patient does have lymphoma, chances for cure are best when it is still localized. Fever, sweats, weight loss or anemia may be seen with certain types of lymphoma. These

Continued on Page 227



CONTINUING MEDICAL EDUCATION IN MAINE

Conferences and Workshops

Title: Family Medicine Update
Date: September 7-10, 1980
Location: Spruce Point Inn, Boothbay Harbor
Sponsors: AAFP and Medical Care Development
Credit: AMA and LCCME Category I—25 hours and AAFP (prescribed)—14 hours
Reg. Fee: \$150; \$210 for State of Maine AAFP members
For further information contact Gerald Goold, Medical Care Development; 622-7566.

Title: Practical-Clinical Cardiology Conference
Date: September 26-28, 1980
Location: Auditorium, Jackson Laboratories, Bar Harbor
Sponsor: American Heart Association, Maine Affiliate
Credit: AMA and LCCME Category I—12½ hours and AAFP (elective)—5 hours
Reg. Fee: To be determined

Title: Third Annual Infectious Diseases Symposium
Date: September 27, 1980
Location: Schaeffer Theater, Bates College
Sponsors: St. Mary's General Hospital, Central Maine Medical Center, and Bates College
Credit: AMA and LCCME Category I—6 hours and AAFP (elective) 6 hours
Reg. Fee: \$10.00

Title: Tri-State Surgical Association Annual Meeting
Date: November 6-9, 1980
Location: Castle Harbor Hotel, Bermuda
Sponsor: Maine Chapter, American College of Surgeons
Credit: AMA and LCCME Category I—18 hours
Reg. Fee: To be determined
For further information contact John Towne, M.D.; 872-7713.

Programs Sponsored By Mid-Maine Medical Center/Colby College

Title: Dermatology for the Non-Dermatologist
Date: July 24-28, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—16 hours

Title: Neurosurgical Techniques
Date: July 27-30, 1980
Credit: AMA and LCCME Category I—21 hours

Title: Otolaryngology
Date: August 3-7, 1980
Credit: AMA and LCCME Category I—18 hours

Title: Epilepsy
Date: August 5-8, 1980
Credit: AMA and LCCME Category I; AAFP—18 hours

Title: Ophthalmology
Date: August 10-14, 1980
Credit: AMA and LCCME Category I—18 hours

Title: Nuclear Medicine

Date: August 17-21, 1980
Credit: AMA and LCCME Category I—28 hours
Title: Medical and Surgical Emergencies
Date: August 19-22, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—25 hours

Title: Forensic Science
Date: August 24-27, 1980
Sponsors: In cooperation with the National Association of Medical Examiners

Credit: AMA and LCCME Category I; AAFP—24 hours

Title: Pulmonary Disease

Date: August 24-28, 1980

Credit: AMA and LCCME Category I—21 hours

All of the Colby activities will be based at the Colby College campus in Waterville. Registration fee is to be determined. For further information contact Robert Kany, Ph.D., Colby College; 873-1131 Ext. 267/251.

Hospital Activities

Augusta General Hospital Augusta, Maine

July 22, 1980 **Hypothermia**
7:30-8:30 a.m. Murray Hamlet, M.D., Army Institute of Environmental Medicine, Natick, Massachusetts

July 29, 1980 **Tumor Conference**
7:30-8:30 a.m. Speaker and topic to be announced
These programs have been certified AMA and LCCME Category I and AAFP (prescribed). ITS presentation. For further information contact Mrs. Nancy Favorite; 623-4711.

Central Maine Medical Center Lewiston, Maine

August 16, 1980 **Amenorrhea—Galactorrhea**
12 Noon Donald Columbus, M.D., Central Maine Medical Center

Every Thursday **Tumor Board** 12-1 p.m.

Every Friday **Medical Grand Rounds** 9-10 a.m.

4th Friday **Joint Surgical Grand Rounds** 7:45-8:45 a.m.
(Odd Months)

2nd Fridays **Visiting Professorship, Boston University** 1-3 p.m.

All activities have been certified AMA and LCCME Category I. For further information contact Carol Murrell, Central Maine Medical Center; 795-2435.

Eastern Maine Medical Center Bangor, Maine

Every Mon. EEG Conference 12-1 p.m.
Every Mon. Surgical Service—Chief's Rounds 5-6 p.m.

4th Mon.	ENT Section Meeting	12-1 p.m.
4th Mon.	Neurosurgery Section Meetings	4-5 p.m.
3rd Tues.	Dermatology-Pathology Conference	5-6 p.m.
3rd Tues.	Dermatology Section Meeting	6-7 p.m.
4th Tues.	Pulmonary Medicine Section Meeting	8-9 a.m.
1st Wed.	Hematology/Oncology Meeting	8-9 a.m.
Every Wed.	Tumor Clinic Conference	2-5 p.m.
Every Wed.	Radiology Conference	5-6 p.m.
	(1) Ultrasound/Nuclear Medicine	
	(2) Radiology Film Review	
	(3) Neuroradiology	
	(4) Teaching File Conference	
	(5) G.I. Radiology	
1st Thurs.	Ophthalmology Section Meeting	7:30-8:30 a.m.
	OB-GYN Conference	8-9 a.m.
	(1) Pathology	
	(2) GYN Analysis	
	(3) OB-Pediatric Combined	
	(4) In-Service and Education	
Every Thurs.	Pediatric Grand Rounds	9-10 a.m.
Every Thurs.	Medical Service Conference	10-11 a.m.
Every Thurs.	Cardiology Conference	11 a.m.-1 p.m.
2nd Thurs.	Orthopedic Grand Rounds	7:45-8:45 a.m.
4th Thurs.	Orthopedic Service Meeting	7:30-9 a.m.
4th Thurs.	Surgical Service Death Review	7:45-8:45 a.m.
Every Thurs.	Psychiatric Service Grand Rounds	10-11 a.m.
4th Thurs.	Urology Section Conference	7:30-8:30 a.m.
Every Fri.	Neurology Grand Rounds	8-9 a.m.

Visiting Professor Program:

2nd Thurs.	Medical Service Visiting Professor	10 a.m.-5 p.m.
2nd Thurs.	Anesthesia Service Visiting Professor	7-8 a.m.
3rd Thurs.	OB/GYN Service Visiting Professor	10 a.m.-4 p.m.
Saturdays	Surgery Service Visiting Professor	8 a.m.-Noon
4th Thurs.	Pediatric Service Visiting Professor	10 a.m.-5 p.m.

as scheduled Orthopedic Service Visiting Professor

as scheduled Family Practice Visiting Professor

as scheduled Psychiatric Service Visiting Professor

All activities have been certified AMA and LCCME Category I. For further information contact James F. Lawsing, III, M.D., Coordinator, Medical Education Committee; 947-3711 Ext. 2303.

A. R. Gould Memorial Hospital Presque Isle, Maine

Every Thurs. Tumor Conference
8 a.m.

2nd Thurs. Perinatal Conference
11:30 a.m.

1st and Tumor Conference
3rd Fri.

The tumor conferences will be held in the Rotary Regional Educational Center and the perinatal conference will be held in Conference Room A. These conferences have been certified AMA and LCCME Category I. For further information contact Marilyn Dean; 769-2511.

Maine Medical Center Portland, Maine Special Conferences

Title: **Michael G. Waddle and David Fournier Memorial Lectures on Hypothermia and Cold Water Immersion**
Date: September 11, 1980
Location: New Diagnostic Facility Classrooms #3 & 4

Sponsors: Emergency Medical Services; American Trauma Society, Maine Division; and Maine Medical Center
Credit: AMA and LCCME Category I—3 hours
Reg. Fee: None
Title: **Albert Aranson Teaching Day**
Date: October 24, 1980
Location: New Diagnostic Facility Classrooms #3 & 4
Sponsor: Maine Medical Center
Credit: AMA and LCCME Category I—3 hours
Reg. Fee: None

Hospital Activities

Every Mon.	Student Technologist Conference	8 a.m.
Every Mon.	Hematology-Pathology Conference	11 a.m.
Every Mon.	Pulmonary Conference	12 Noon
Every Mon.	Pediatric Residents' Conference	1 p.m.
Every Mon.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Mon.	Surgical Pathology Review	4 p.m.
Every Mon.	Radiology Journal Club	5 p.m.
1st &	Clinical Nephrology Conference	11 a.m.
3rd Mon.		
1st &	Hematology-Pathology Conference	12 Noon
3rd Mon.		
3rd Mon.	Eye Conference	11:45 a.m.
Every Tues.	Radiology Residents' Seminar	7 a.m.
Every Tues.	Family Practice Grand Rounds	9 a.m.
Every Tues.	Electrocardiographic Interpretation	1 p.m.
Every Tues.	Psychiatric Grand Rounds	1:30 p.m.
Every Tues.	Anesthesia Formal Resident Lecture	3:30 p.m.
Every Tues.	Surgical Seminar	4 p.m.
Every Tues.	Pathology Slide Seminar	4 p.m.
1st &	Radiology-Pathology Conference	12 Noon
3rd Tues.		
1st &	Neurology Conference	12 Noon
4th Tues.		
2nd Tues.	Infectious Disease Conference	12 Noon
3rd Tues.	Hematology Conference	12 Noon
5th Tues.	Oncology Conference	12 Noon
Every Wed.	Radiation Therapy Conference	7 a.m.
Every Wed.	Urology Conference	7 a.m.
Every Wed.	Student Technologist Conference	8 a.m.
Every Wed.	Continuing Education Seminar	8 a.m.
Every Wed.	Medical Conference	9 a.m.
Every Wed.	Psychiatric Journal Club	12 Noon
Every Wed.	Cardiology Seminar	12 Noon
Every Wed.	Surgical Grand Rounds	5 p.m.
2nd Wed.	Guest Internist—Medical Conference	9 a.m.
4th Wed.	Medical Mortality Conference	9 a.m.
Alt. Wed.	Neurology-Psychiatry Seminar	11 a.m.
Alt. Wed.	Anesthesiology Journal Club	3 p.m.
Every Thurs.	Thoracic Surgery Conference	7 a.m.
Every Thurs.	OB/GYN Conference	7 a.m.
Every Thurs.	Anesthesiology Clinical Conference	7 a.m.
Every Thurs.	Diagnostic Radiology Teaching Conference	7 a.m.
Every Thurs.	Surgical Conference	8 a.m.
Every Thurs.	Pediatric Conference	9 a.m.
Every Thurs.	Tumor Consultation Board	11 a.m.
Every Thurs.	Medical Residents' Conference	12 Noon
Every Thurs.	Surgical Seminar	4 p.m.
Every Thurs.	Endocrinology Conference	5 p.m.
Every Thurs.	Dental Specialty Lecture	6 p.m.
1st Thurs.	Anesthesia Mortality Conference	7 a.m.
1st Thurs.	Guest Pediatrician	9 a.m.
1st Thurs.	Gastroenterology Conference	12 Noon
1st &	Cardiac-Surgical Conference	12:30 p.m.

3rd Thurs. 1st, 3rd, & 5th Thurs.	Pulmonary-Physiology Conference	12:30 p.m.
2nd Thurs.	Cardiology Teaching Conference	12:30 p.m.
2nd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
2nd Thurs.	Eye Staff Scientific Session	5:30 p.m.
2nd Thurs.	Maine Medical Center Medical Staff Meeting and Scientific Session	6 p.m.
2nd & 4th Thurs.	Pulmonary-Pathology Conference	12 Noon
2nd & 4th Thurs.	Endocrinology Conference	12 Noon
3rd Thurs.	Combined Guest Physician or Guest Surgeon Program	8 a.m.
3rd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
4th Thurs.	Surgical Mortality Conference	8 a.m.
4th Thurs.	Anesthesia Mortality Conference	3:30 p.m.
Last Thurs.	Pediatric Mortality Conference	9 a.m.
Every Fri.	Thoracic-Surgical Conference	7 a.m.
Every Fri.	Nuclear Medicine Conference	7 a.m.
Every Fri.	Student Technologist Conference	8 a.m.
Every Fri.	Neurological-Neurosurgical Conference	8:30 a.m.
Every Fri.	Gastroenterology Conference	9 a.m.
Every Fri.	Medical Rehabilitation Staff Conf.	9 a.m.
Every Fri.	Orthopedic Conference	9 a.m.
1st Fri.	Dermatology Conference	12 Noon
2nd Fri.	Nephrology Conference	12 Noon
3rd Fri.	Rheumatology Conference	12 Noon
4th Fri.	Oncology Conference	12 Noon
Alt. Fri.	Oncology-Radiation Conference	7 a.m.
Alt. Fri.	Gastroenterology Conference	10 a.m.

All programs have been certified AMA and LCCME Category I. For further information contact Costas T. Lambrew, M.D.; 871-2111.

Mid-Maine Medical Center Waterville, Maine

July 24, 1980	Chronic Low Back Pain—Recent Developments John S. Diggs, M.D., Mid-Maine Medical Center
July 31, 1980	Case Presentation Family Practice Residents
August 7, 1980	Clinical Pathological Conference (Medical Staff only)
August 14, 1980	Orthopedics Stuart Belkin, M.D., Tufts University School of Medicine, Boston
August 21, 1980	Newer Agents in RX of Hypertension Paul Parker, M.D.
August 28, 1980	Case Presentation Family Practice Residents
Every Mon.	Ophthalmology 8-10:30 p.m.
Every Tues.	Tumor Board 12 Noon-1 p.m.
Every Tues.	Regional Infectious Disease ITS presentation 12 Noon-1 p.m.
3rd, 4th,	Obstetrics with Augusta 12 Noon-1 p.m.

& 5th Tues.	General Hospital	
Every Wed.	Regional Pulmonary Disease ITS presentation	12 Noon-1 p.m.
Every Thurs.	Medical-Surgical Conference	12 Noon-1 p.m.
Thurs.-Weekly	Regional Pathology	1-2 p.m.
Thurs.-Monthly	Department of Medicine	6-7:30 p.m.
Every Fri.	Anesthesiology	6:30-7:30 a.m.
Every Fri.	Orthopedics	7-8 a.m.
Every Fri.	Pediatrics	12 Noon-1 p.m.
2nd Fri.	General Surgery	7-8 a.m.
4th Fri.	Surgical Audit	12 Noon-1 p.m.

All activities have been certified AMA and LCCME Category I. The Medical-Surgical Conference on Thursday has also been certified AAFP (elective). All are ITS presentations excluding CPC. For further information contact David R. Ginder, M.D.; 873-0621.

Penobscot Bay Medical Center Rockland, Maine

July 25, 1980 **Ophthalmology Grand Rounds**
Grand rounds is from 11 a.m. to 12 Noon and has been certified AMA and LCCME Category I. For further information contact Lloyd Roberts, M.D.; 594-9511.

St. Mary's General Hospital Lewiston, Maine

Every Tuesday 8-9 a.m.	Medical Grand Rounds
1st and 3rd Fridays 12-1 p.m.	Tumor Conference
Last Friday of month 12-1 p.m.	Surgical Grand Rounds

The Surgical Grand Rounds will be alternating monthly between St. Mary's General Hospital and Central Maine Medical Center. These activities have been certified AMA and LCCME Category I. For further information contact Michael C. Bach, M.D.; 783-2227.

V. A. Hospital Togus, Maine

June 20, 1980 10 a.m.	Therapeutic Approaches to Neuropathies Marilyn R. Kassirer, M.D., Staff Neurologist, Veterans Administration Out-Patient Clinic, Boston VA Hospital
Every Wednesday 1:15-2:15 p.m.	Medical Staff Service Meetings
Every other Thurs. 2-3 p.m.	Oncology Clinic
2nd Tues. of month	Psychiatric CME Meetings

These activities have been certified AMA and LCCME Category I. For further information contact E. Osborne Coates, Jr., M.D., VAM and ROC, Togus; 623-8411.

ANNOUNCEMENT: Medical Care Development, Inc. is now receiving a listing of continuing medical education activities taking place in Vermont, New Hampshire, and Massachusetts. If you wish further information contact Gerald Goold, Medical Care Development; 622-7566.

There was no correspondents or miscellaneous business to be presented.

There were 21 physicians and 1 guest present.

The meeting was then adjourned.

MELVIN BACON, M.D., *Secretary*

Kennebec

The Kennebec County Medical Association met at the Silent Woman Restaurant in Waterville on February 21, 1980.

The Secretary was unable to attend due to illness. The program was a presentation of strength of the U.S. Navy. All business for that month was deferred due to my absence.

The Kennebec County Medical Association met at the Silent Woman Restaurant in Waterville on April 17, 1980 with 47 members and guests in attendance. After a most pleasant cocktail hour and delicious dinner of a choice of baked stuffed pork chops or fillet of sole, the business session was held.

The following business consisted of: Election of Dr. John Engle and reading of the applications of Drs. Zacharias Matthews, David Jones and Donna Conkling. Dr. Towne then introduced our speaker, Roger Zimmerman, who gave a very nicely prepared talk on the subject of sex therapy.

The meeting adjourned at 9:30 p.m.

O. THOMAS FEAGIN, M.D., *Secretary*

Oxford

A meeting of the Oxford County Medical Society was held on March 12, 1980 at the Madison Motor Inn in Rumford. Eighteen active members were in attendance. Dinner was enjoyed by members and their spouses.

The meeting was called to order by the President of the Society; Dr. Linwood M. Rowe.

It was decided by the County Society members that Dr. Li, who was an active member of the Society and who is now retired, be recommended for affiliate membership. A letter to this effect will be forwarded to the Maine Medical Association.

The Preliminary State Health Plan for Maine was reviewed briefly by the members and it was felt that all members should study the plan more thoroughly and then forward our opinions to Maine Medical Association.

Dr. Robert B. Funch gave an excellent presentation on percutaneous transhepatic cholangiography in a community hospital.

The next meeting is scheduled for Wednesday, May 14, 1980, and is to be held in South Paris, Maine.

There being no further business, the meeting was adjourned.

USHA WADHERA, M.D., *Secretary*

Androscoggin

A meeting of the Androscoggin County Medical Association was held on March 20, 1980 at Chase Hall, Bates College in Lewiston with 51 members present. The guest and featured speaker for the evening was Dr. Robert McAfee, of Cumberland County, President-elect of the M.M.A. and the M.M.A. Delegate to the A.M.A.

The meeting was called to order by the President, Dr. Leo Cousineau at 7:30 p.m.

Printed minutes of the meeting held February 21, 1980 were distributed and accepted.

Dr. Walworth reviewed the minutes of the previous Executive Committee meetings and Dr. Frederick Holler briefly discussed the BC/BS questionnaire regarding HMOs. Also discussed was the question of whether osteopaths could apply for membership to county medical associations.

Dr. Gilbert Grimes then gave an update of the financial status of the M.M.A.

Dr. Cousineau announced that Dr. Andre Marcotte had been named chairman of the PTO-PSR nominating committee and that Dr. Roger Austin has been nominated to the Board.

Dr. Cousineau also announced that all members nominated to the Advisory Board had accepted and that this committee is to

convene in the near future and will report to the Association at the April meeting.

Discussion ensued as to the recent hearing on the Preliminary State Health Planning Report. Dr. Barry Chandler gave a brief history of the (Maine) State Health Coordinating Council of which he has been a member. Dr. Grimes will send a letter to Governor Brennan in regards to the Preliminary State Health Plan on behalf of the ACMA.

Dr. Norman Chazin reported on the status of a proposed psychiatric hospital and will keep the Association informed of any new developments.

Dr. Robert McAfee then addressed the Association on issues facing local physicians in the near future and on the A.M.A. Code of Ethics.

The meeting adjourned at 9:35 p.m.

EDWARD Z. WALWORTH, M.D., *Secretary*

Knox

The Knox County Medical Society met at the Sail Loft Restaurant in Rockport on April 1, 1980 with twenty-eight members in attendance. Invited guest was Dr. Dan Hanley.

A motion was brought and seconded and passed to suspend business discussion at this point in time and proceed directly with the guest speaker. Dr. Edward Morse presented Dr. Hanley with a gift of appreciation from the Knox County Medical Society for his years of service to the Maine Medical Association and Knox County Medical Society. Dr. Hanley then proceeded with an informative and entertaining lecture on the early beginnings of the Maine Medical Association.

The meeting was adjourned at 9:30 p.m.

ALBERT J. LANTINEN, JR., M.D., *Secretary*

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News, Notes and Announcements

American Heart Association Maine Affiliate Presents 31st Annual Scientific Session

PRACTICAL CLINICAL CARDIOLOGY CONFERENCE

by W. Proctor Harvey, M.D., F.A.C.C.

*To be held in the auditorium of The Jackson Laboratory,
Bar Harbor, Maine
September 26, 27 & 28, 1980*

Friday Evening September 26, 1980

5:00 p.m.-7:30 p.m. Registration
7:30 p.m.-10:00 p.m. Lecture: Cardiac Pearls

Saturday Morning September 27, 1980

8:00 a.m.-12:30 p.m. Interrelations of auscultation with the physical examination and the total cardiovascular evaluation. Heart sounds: Normal and abnormal including splitting of sounds, clicks, gallop, rhythms and sounds in diastole with patient presentations.

Saturday Afternoon Elective

2:00 p.m. - 4:30 p.m. Cardiac diagnosis using multimedia system

5:30 p.m. Cocktails

6:30 p.m. - 7:00 p.m. Presentation of Eugene Drake Award

7:00 p.m. Banquet

Sunday Morning September 28, 1980

8:00 a.m.-12:30 p.m. Acquired and Congenital Heart Disease Classifications and Hemodynamic Correlations Surgical Risk

Sunday Afternoon Elective

2:00 p.m.-4:30 p.m. More Cardiac diagnosis using multimedia system

registration limited, early registration encouraged

W. Proctor Harvey, M.D., F.A.C.C., Professor of Medicine,

Georgetown University School of Medicine; Director of Division of Cardiology, Georgetown University Medical Center, Washington, D.C.

State of Maine Department of Human Services Division of Child Health Clinic Schedule—1980

By Appointment Only

Orthopedic Clinics

Bangor—St. Joseph Hospital

9:00 a.m.: Mar. 27, Apr. 24, May 22, June 26, July 24, Aug. 28, Sept. 25, Oct. 23, Nov. 20, Dec. 18

Fort Kent—Northern Maine Medical Center

9:00 a.m.: Mar. 11, May 13, July 15, Sept. 9, Nov. 4

Houlton—Houlton Regional Hospital

10:00 a.m.: Mar. 10, May 12, July 14, Sept. 8, Nov. 3

Presque Isle—A.R. Gould Memorial Hospital

9:00 a.m.: Mar. 12, May 14, July 16, Sept. 10, Nov. 5

Waterville—Mid-Maine Medical Center (Seton Unit)

Time scheduled by hospital: Mar. 3, Apr. 7, May 5, June 2, Sept. 8, Oct. 6, Nov. 3, Dec. 1

Cleft Palate Clinic

Portland—Maine Medical Center

9:00 a.m.: Mar. 17, May 19, June 16, Sept. 15, Oct. 20, Nov. 17

Cardiac Clinics

Bangor—St. Joseph Hospital

9:00 a.m.: Mar. 14, Apr. 11, May 9, June 13, July 11, Aug. 8, Sept. 12, Oct. 10, Nov. 14, Dec. 12

Portland—Maine Medical Center

9:00 a.m.: Mar. 7, 14, 21, 28, Apr. 4, 11, 18, 25, May 2, 9, 16, 23, June 6, 13, 20, 27, July 11, 18, 25, Aug. 1, 8, 15, 22, Sept. 5, 12, 19, 26, Oct. 3, 10, 17, 24, Nov. 7, 14, 21, Dec. 5, 12, 19

Children's Development Clinic

Lewiston—Central Maine Medical Center

8:30 a.m.: Mar. 10, Apr. 14, May 12, June 9, July 14, Aug. 11, Sept. 8, Nov. 10, Dec. 8

DIAGNOSTIC IMPERATIVES IN INTERNAL MEDICINE—Continued from Page 222

findings suggest a poorer prognosis and usually call for aggressive treatment. The choice of specific therapy, however, still depends on the histologic diagnosis. Proper therapy of lymphoma is usually effective in eliminating, at least transiently, signs and symptoms, even in the sickest patients. In a proportion of patients, cure may be achieved.

When splenomegaly occurs without adenopathy or liver disease, there is more of a dilemma. If the patient is well and free of clinical and laboratory evidence of disease, there may be little advantage to pursuing the finding. If there are symptoms related to the size of the spleen or if cytopenias are present, further studies should be done. A liver-spleen scan is helpful in ruling out delayed rupture of the spleen or cyst (an old rupture), in documenting liver size, and to some extent demonstrating liver function. Liver biopsy often provides a window to the spleen and in

general should be done before splenectomy is considered both to rule out the possibility of cirrhosis and to demonstrate other diseases such as lymphoma which may be involving the spleen. The final decision for splenectomy depends on the clinical problem. If there is associated cytopenia of severe degree, e.g., pronounced neutropenia with infection in Felty's syndrome, splenectomy is a reasonable therapeutic measure. If there is a rapidly enlarging spleen in a patient in whom all studies are normal, it is reasonable to proceed with splenectomy; the most likely diagnosis in this case is lymphoma but one would not treat for such an illness without having histologic confirmation. If splenomegaly is an incidental finding in an otherwise healthy person, one may choose instead to wait and observe. In general, then, associated clinical findings determine the appropriate approach in managing a patient with splenomegaly.

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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d. alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed, adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d., adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

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well controlled. In public issues, however, we deal with perceptions which may be irrational, but are nevertheless real public problems.

We can only follow the guidelines we adhere to in all other areas—to look at the scientific and medical evidence, to take rational positions based on this evidence always from the point of view of the safety of our patients.

Reports of Reference Committees—Recommendations (not listed elsewhere in this summary) are as follows:

Committee on Conservation of Vision—Accepted and referred to the Maine Society of Eye Physicians and Surgeons.

Committee on Continuing Education—The report was approved and referred to the Executive Committee for consideration.

Diabetes Committee—Referral to the Executive Committee for review was approved.

Maternal and Child Welfare Committee—Number 1 under the Summary of Task Force Recommendation (regarding the question of the aegis under which the review committee be established) was referred to the Executive Committee. With the exception of this one aspect of the report, the report was accepted.

Recruitment, Aid & Placement—Referred back to the Committee; report to be re-submitted at a later date for review.

A. H. Robins Award was presented to Dr. Linus J. Stitham of Dover-Foxcroft.

Maine Blue Cross and Blue Shield Award of Appreciation was presented this year to Dr. Charles H. Lightbody of Guilford.

Out-of-State Delegates—The following delegates spoke briefly and extended greetings on behalf of their societies: Benjamin M. Shenker, M.D., Connecticut; William H. Gifford, M.D., New Hampshire; Robert L. Conrad, M.D., Rhode Island; John Leppmann, M.D., Vermont, and Donald R. Hayes, M.D., Massachusetts.

Special Memberships—The recommendations by the county societies were approved.

Other—Discussion of the Medicaid ruling relative to reimbursement for sterilization without a sterilization form was referred to the Committee on Health Care.

The meeting was recessed at 3:15 P.M. on Thursday, June 12, and was adjourned at 5:45 P.M. on Friday, June 13.

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Editorial

Calcium Flux Antagonists

A New Treatment for Some Patients With Angina Pectoris?

Since first proposed by Heberden, the role of coronary artery spasm as a cause of angina pectoris has been disputed, primarily because of the inability to document its presence.¹ The demonstration by pathologists of the sclerotic obstructing lesions in the coronary arteries of patients with angina distracted our attention from the concept of spasm as a cause for this pain. We became preoccupied instead with our ability to demonstrate the exact location and extent of the coronary arterial disease by angiography.

Recently, as a result of the work of Maseri and his colleagues in Italy, our attention has again been directed to the occurrence of coronary artery spasm in patients with angina pectoris.² Numerous studies have now confirmed the role of coronary artery spasm in producing the pain experienced by those patients with typical Prinzmetal's Angina. In addition, coronary artery spasm may be responsible for the development of chest pain and even myocardial infarction in patients with typical obstructing arteriosclerotic coronary artery disease.⁴

Calcium flux antagonists, a new class of vasodilator drugs, are being tested extensively in patients with angina pectoris. These drugs inhibit vascular spasm in the coronary arterial bed by blocking the transmembrane flux of calcium, an ion required for smooth muscle contraction.⁵

Nifedipine, one of the calcium flux antagonists, has been tested extensively during the past several years for the treatment of angina patients in Europe, Latin America, Japan and the United States.

The results of these trials are preliminary but so far very encouraging and the adverse side effects are minimal and well tolerated.³ As expected, the benefits are most striking for those patients with typical coronary artery spasm, but surprisingly good results are also seen in patients with stable exertional angina.³ Our experience at Eastern Maine Medical Center with Nifedipine since 1979 has been similar to that reported by other clinical investigators.

The results of Maseri's work and the expectation of a new form of treatment has encouraged us all to look more carefully for those patients in whom coronary artery spasm might be a contributing cause for their angina. Patients with chest pain at rest should have a twelve lead electrocardiogram during the chest pain to look for the characteristic ST segment elevation, and careful note should be made of the blood pressure and heart rate response. At the present time, aggressive treatment with nitrates is helpful for many of these patients. The initial results of studies using calcium flux antagonists suggest that in patients with coronary artery spasm these new drugs may be even more helpful.

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Proximal Control in Ruptured Abdominal Aortic Aneurysms

DAVID M. SENSENIG, M.D.*

Ruptured abdominal aortic aneurysm presents an extremely serious emergency requiring prompt surgical treatment. Of those patients reaching the hospital, only about fifty percent survive. While blood is being crossmatched, the patient should be taken to the operating room where control of aortic bleeding should be promptly undertaken.

Several different methods of proximal aortic control have been advocated. Temporary clamping of the aorta above the diaphragm via left thoracotomy has been recommended. We have not used this method because of the necessity of opening another body cavity and the difficulty of reaching the thoracic aorta unless the patient was rotated.

Usually we have mobilized the aorta as it comes through the diaphragm and then temporarily clamped it until another clamp could be placed across the aorta above the aneurysm and below the renal vessels. This method is outlined in *Techniques in Vascular Surgery* by Denton Cooley and Don C. Wukasch.¹ Linton² has recommended opening the aneurysm and inserting the thumb into the neck of the aneurysm until control can be achieved.

Both of the above methods generally require the induction of general anesthesia and then a rapid dissection. All preparation and draping can be done prior to inducing the anesthetic so that control can be achieved as rapidly as possible. Unfortunately, in our experience, the patient can go rapidly into shock with the induction of general anesthesia which reverses the intense peripheral vasoconstriction which has maintained blood pressure in the face of hypovolemia. During this hypotension, the patient may suffer a coronary artery occlusion, damage to the kidney or brain, or even cardiac arrest.

Recently, we have employed another method using local anesthesia which has enabled us to control the aneurysm. In this way, there is much less fall in blood pressure when general anesthesia is induced so that adequate time is provided to accomplish cross clamping below the renal arteries.

In this method, the abdomen and upper thighs are prepared and draped while all instruments are in readiness and the anesthesiologist is prepared to induce anesthesia when the proper time arrives. One of the femoral arteries is exposed under local anesthesia. Ten thousand units of aqueous heparin are injected intravenously. After about a three-minute wait to permit adequate mixing, the common femoral artery is clamped distally. An incision in the artery is then made and a Fogarty intra-aortic balloon catheter

is passed up the iliac artery and through the aneurysm into the distal thoracic aorta much as an angiographic catheter would be passed for preoperative angiography in an elective case. When in the thoracic aorta, the balloon is inflated with about 43 ml. of saline or enough to occlude the aorta. As the balloon is inflated, the abdominal aortic pulsation ceases. After the aorta is occluded in this manner, general anesthesia is induced and a long mid-line incision is made to expose the aneurysm. The occlusion of the lower thoracic aorta not only controls bleeding but reduces the vascular bed thereby maintaining blood pressure while blood is rapidly infused. It is now much simpler to isolate the neck of the aneurysm and clamp it than it would be in the face of a pulsating aorta and hematoma. After the clamp is around the aorta, but prior to closing it, the intra-aortic balloon is deflated and withdrawn.

We have found this method to be helpful and recently used it to facilitate a successful resection of a ruptured aneurysm in an elderly man. In a more recent instance, we could not pass the balloon up the right iliac artery so we induced anesthesia and inserted the balloon through the wall of the aneurysm. This case had a successful outcome as well. We might have been successful passing it up the other femoral and iliac artery. It would seem wise to try both sides before losing the advantage of aortic control prior to the induction of general anesthesia.

SUMMARY AND CONCLUSIONS

A method of controlling the aorta under local anesthesia in cases of ruptured abdominal aortic aneurysm is presented.

After systemic heparinization, and intra-aortic balloon catheter is passed up into the lower thoracic aorta from the femoral artery which is exposed after infiltration with one percent Xylocaine.[®]

After inflating the balloon and controlling bleeding, general anesthesia is induced and the neck of the aneurysm is exposed.

The balloon catheter is then withdrawn and the aorta clamped below the renal arteries and above the aneurysm.

This method minimizes the chance of vascular collapse with subsequent bad effects such as cardiac arrest, renal damage, stroke and coronary artery occlusion.

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The Use of Methylene Blue Solution to Test for Leaks in Gastric Bypass Operations for Morbid Obesity

DAVID M. SENSENIG, M.D. AND H. CLEMENT JURGELEIT, M.D.*

Throughout the country an ever-increasing number of gastric bypass operations are being performed as good results in effecting weight loss are achieved. Safety is especially important in this group of patients who are for the most part under fifty years of age in their most productive years. An important cause of mortality in published series¹ is anastomotic leak at the site of gastrojejunostomy. Assuming a good blood supply and no excessive tension it is unlikely that an anastomosis will leak if there is none at the time of operation. We have found that a simple test with saline colored with methylene blue has been helpful in detecting a leak in the anastomosis as constructed at operation.

METHOD

By and large, we have fashioned a gastric pouch holding about 30 to 40 cc. using the Auto-Suture TA 90 with 4.8 mm. staples. That pouch is drained with a loop of jejunum making an anastomosis about 1.5 cm. in diameter using the Auto-Suture GIA instrument and closing the stab wounds by an inner layer of 3-0 continuous locking catgut and an outer layer of interrupted 3-0 silk. A large enteroenterostomy is made between the ascending and descending limbs in the same manner. After constructing the first anastomosis, we instruct the anesthetist to inject about 60 or more cc. of saline containing methylene blue into the stomach pouch via the nasogastric tube as we obstruct the ascending and descending limbs of jejunum. As the stomach and jejunum balloon up, we have an opportunity to detect any leak. After the second anastomosis, a second test is done using about 100 or more cc. to check the lower anastomosis.

RESULTS

Since December of 1978, the methylene blue test has been used in 30 patients undergoing gastric bypass. We found it to be easy to perform and very useful. For example, in one patient a small leak of

the stab wound closure at the upper anastomosis was detected and repaired. In a second patient, the GIA stapler had crossed a large hemoclip causing inaccurate placement and closure. This defect was readily identified and repaired. In a third patient, a post-operative leak from the gastric fundus was caused by a nasogastric tube which had been deflected upward by the staple closure line. At the time of re-operation, it was easy to identify this small perforation with the methylene blue solution and close the leak. In a fourth patient, a small amount of dye was seen under the seromuscular closure where the catgut closure line leaked. This prompted the placement of additional seromuscular sutures to achieve a secure anastomosis.

DISCUSSION

The challenge of an anastomosis high in the abdomen where leaks are difficult to detect led us to use the methylene blue test with subsequent satisfaction. It has prevented peritonitis and possible death from an otherwise undetected leak. The principle can be used to advantage in other areas where leaks are a danger such as esophagocolostomy in colon transplant cases. We recently proved that an esophagocolic anastomosis was tight with this test. Likewise, it could be used in low anterior resection injecting the blue solution into the colon with a needle and syringe and then closing the small needle tract after the test.

SUMMARY AND CONCLUSION

The injection of methylene blue dyed saline solution to detect anastomotic leak after intestinal anastomosis in the gastric bypass operation for obesity has proven helpful in detecting leaks in four of 30 cases. We recommend its use in these operations as well as in other anastomoses where leak is a hazard such as esophagogastrostomy, esophagocolostomy and low anterior resection of the rectum.

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Differential Diagnosis of Chest Pain—With Known Coronary Heart Disease

WILBUR B. MANTER, M.D.*

I have chosen this subject on premises that: ischemic heart pain for a given individual patient remains similar in quality if and as it may recur, that patients who have or have had ischemic pain often have chest pain due to other causes, that failure to make correct differential diagnosis is not an infrequent cause for failure of these patients to return to as full capacity as treatment of their coronary disease makes possible. I might add that both ourselves, as physicians, and our patients will benefit and learn much in the course of the careful, albeit time-consuming inquiry required for this differential diagnosis.

The goal in management of the patient who has diagnosed symptomatic coronary heart disease is his return to a full and satisfactory lifestyle. Unfortunately, many patients do not return to work or to the lifestyle that the application of recent advances in medical and surgical therapy now make possible. There are various and sometimes complex reasons why this is so, including social and economic. However, for many patients, I believe the cause may be misinterpretation of the significance of chest pain that they often continue to have.

Tinsley R. Harrison, after writing outstanding papers on clinical aspects of chest pain for over 30 years, wrote retrospectively that more than 60% of patients with undoubted angina pectoris also have other causes of chest or shoulder girdle pain.¹

Obviously, non-ischemic pain misinterpreted as angina, an "overload signal," or as an indicator of an acute coronary attack, is a serious upset for the patient who may have an abnormal electrocardiogram, an abnormal exercise test, an abnormal coronary angiogram, and abnormal cardiac nuclear studies. He could have abnormal gastro-esophageal or cervico-dorsal nerve root or other abnormal studies. This serves to emphasize the importance of the careful analysis of chest pain by history in its differential diagnosis—not the newest of techniques in this increasingly technique-oriented time and a subjective technique in this time of increasing demand and means for objective confirmation for diagnosis. Thomas Addison said 130 years ago, referring to the stethoscope: "This new tool will prove invaluable provided it does not lead to neglect of ...careful and minute inquiries..."¹

I would like to discuss some points that have been helpful to me in managing patients with identified

and treated symptomatic ischemic heart disease, who also have or develop non-cardiac chest pain.

First, once I feel I can identify a patient's ischemic pain, I make a note in a conspicuous part of the record on the location, including radiation, but particularly on the quality of the pain in the patient's words, for future reference.

Although the severity, the degree of radiation, and occasionally the order of radiation of the pain may vary, I believe it rare for the basic quality of ischemic pain to change for a given individual. I find that the patient can better recall this particular pain in the future if reference can be made to it by a key descriptive word or two of his own—sometimes words I would not ordinarily have considered appropriately descriptive. Beware of words that may have been supplied by yourself or others, for pain description. It is sometimes surprising to ask a patient what he means by stock words as "crushing," or "vise-like."

Not a few patients whom I conclude have had ischemic pain deny this as pain—they did not consider what had come out as heaviness, pressure, indigestion or sense of difficulty breathing as pain. Occasionally, the familiar hand sign may be the descriptor. I wonder if some of the "painless" myocardial infarctions are not in this group.

Also I believe an occasional patient had non-ischemic pain that was the pain that concerned him at about the time of myocardial infarction. His true ischemic pain may have been considerably less uncomfortable and he may not have voluntarily described it.

When trying to get a differential in quality of pains, especially when comparing a similarly located pain with the presumed ischemic pain of the past, and the patient doesn't understand me, I find it may be helpful to illustrate a difference as by varying degrees of a pin-prick and application of pressure in a same area, while saying pains due to different causes may occur in the same place, but can feel different regardless of severity.

Pains related to various wall structures, including those of nerve root origin, are frequent but with their quality and location, tenderness, aggravation by various motions, and other features, they usually are not difficult to differentiate from ischemic pain. Most of these pains for the patients I see, are not due to serious underlying cause, and assurance is usually the important, if not the only treatment necessary. Most often I don't manage to have a specific diagnosis for these pains that I usually classify as "chest wall pain."

The "shoulder-hand" syndrome, so-called reflex

Continued on Page 243

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Ultrasound Guided Percutaneous Nephrostomy with Fluoroscopic Assistance

DON E. FACTOR, M.D.*

INTRODUCTION

Percutaneous renal drainage has been described since 1955, and has evolved from a test of residual renal function in obstruction to a proven useful easily performed method of treatment that can be comfortably tolerated by very ill patients.

INDICATIONS

Percutaneous nephrostomy is the initial treatment of choice for severe obstructive renal failure which is usually bilateral. This procedure provides time to properly prepare the patient for definitive surgery, to deliver chemotherapy or radiotherapy, or to allow edema to subside from a calculus. With pyonephrosis and septicemia, the relief of obstruction can assist clinical improvement in 24-48 hours.

Additional time can be gained to evaluate or stabilize a recent myocardial infarction, or inflammatory bowel disease near the anticipated surgery.

The role for drainage has been extended to assist closure of a ureteral fistula, calculus irrigation and extraction access route, drug instillation of bacterial and fungal antibiotics, chemotherapy, and stone dissolving solutions.

TECHNIQUE AND EQUIPMENT USED

Mild sedation with diazepam (Valium®) can be used and the patient is turned in the prone oblique position and the portable C-arm fluoroscope placed. The dilated renal pelvis is localized with an articulated B scan ultrasound or real time unit while the patient is in quiet respiration. When the desired vertical pathway has been decided upon (Fig. 1) after ultrasound scanning, the skin is scratched, anesthetized, and prepared aseptically and draped. The Seldinger technique of needle insertion is used after urine is returned from the needle and guidewire placement is performed. A #18 gauge needle with a #8.3 French pigtail nephrostomy catheter (Cook) are used. The position of the guidewire in the renal pelvis is confirmed by fluoroscopy as it curves as it enters the renal pelvis, or by its course down the ureter. The tract is then progressively dilated to the final catheter size and the pigtail multiple side hole nephrostomy catheter is inserted with a twisting motion and monitored fluoroscopically. The catheter is then fixed to the skin with suture and tape. An antegrade pyelogram confirms the catheter position and outlines the ureter to the point of obstruction. A radiograph is then made for permanent record (Fig. 2).

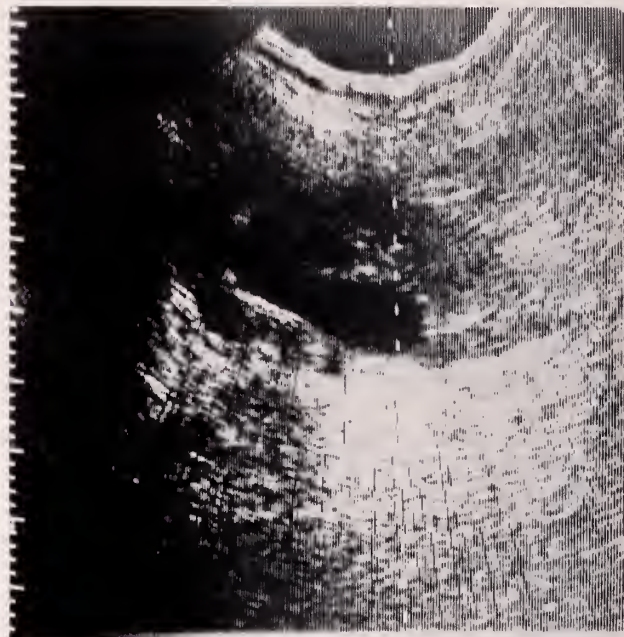


Fig. 1. The dilated renal pelvis is localized with ultrasound and needle path was selected.

DISCUSSION

A few comments are in order in the above technique. The use of ultrasound is valuable to determine the course and depth of puncture and eliminate the need for an initial antegrade pyelogram. The approach from the flank is preferred as the major renal vessels are avoided and the final position of the catheter is more comfortable for the patient when lying supine.

If a permanent (greater than 3 weeks) nephrostomy is desired the tract can be dilated with vascular dilators and a Foley type balloon catheter inserted. Larger catheters such as #12 French may be used to drain pus and for irrigation. Small calculi, fungus balls, and sloughed papillae can sometimes be displaced down the ureter to the bladder. Large uric acid stones and cystine calculi can be dissolved with alkaline infusions. Difficulty is often times encountered with staghorn calculi in minimally dilated calices. Here antegrade pyelography is of value to distend the collecting system before guidewire insertion, however, this should be monitored fluoroscopically.

Antegrade pyelography should not be performed if there is urinary tract infection, as bacteremia can be precipitated. Prophylactic antibiotics or urinary antiseptics can be regularly prescribed depending on the clinical setting. Hematuria is common and it usually

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clears within 24 hours. The success rate of the procedure should approach 97%. Complications such as infection and bleeding are others which may require specific treatment are about 4% in most series.

OUR EXPERIENCE

The ten catheter placements we have performed on six patients is small compared to hundreds reported in the literature, but the results are encouraging. A brief summary follows:

G.B.—Presented with anuria and obstruction from recurrent transitional cell carcinoma of the bladder 2 years after radiotherapy.

M.G. and R.M.—Presented with anuria from retroperitoneal metastasis.

M.W.—Had obstruction from retroperitoneal fibrosis. A nephrostomy was placed until definitive surgery was performed.

K.O.'L.—Had recurrent ureteropelvic junction obstruction and the nephrostomy provided relief until subsequent pyeloplasty was performed.

C.D.—Was treated with a nephrostomy for relief of pain from obstruction due to metastatic colonic carcinoma.

SUMMARY

The Seldinger technique of percutaneous nephrostomy is described. This is a low risk, low morbidity procedure allowing temporary urinary diversion. It should be considered in patients who are not immediate operative risks and in those whom no definitive operative repair is planned.

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Fig. 2. Antegrade pyelogram confirming the nephrostomy tube position in the renal pelvis.

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Pituitary Metastatic Disease

Report of a Case and Review of the Literature

CLIFFORD J. ROSEN, M.D.* AND GALEN R. HASLER, M.D.**

INTRODUCTION

Distant metastasis to the pituitary gland was once considered an autopsy diagnosis. However, it is now known that 1% of breast cancer patients with metastatic disease develop diabetes insipidus.¹ Reports of hypothalamic and/or posterior pituitary metastasis manifested by diabetes insipidus have also been reported in tumors from the lung, GI tract, cervix, pancreas, and kidney.² With the advent of C-T scanning and more elaborate and provocative pituitary testing, relatively asymptomatic pituitary metastasis are being more frequently reported.

Diabetes insipidus is the only clinical manifestation of posterior pituitary involvement. Large metastasis in the suprasellar or pituitary region could conceivably result in anterior pituitary dysfunction as well as diabetes insipidus. However, anterior pituitary metastasis and subsequent clinical endocrine dysfunction are rare antemortem.

We report a case of oat-cell carcinoma of the lung with pituitary metastasis that exhibited diabetes insipidus and clinical signs of anterior pituitary hypofunction. A review of metastatic pituitary disease is also undertaken.

CASE REPORT

A.B. presented with abdominal distress and dyspnea. Evaluation revealed a right lower lobe infiltrate, hepatomegaly, and abnormal liver function studies. Fiberoptic bronchoscopy and biopsy demonstrated occlusion of the bronchus intermedius with small cell undifferentiated carcinoma. Staging bone marrow biopsy and C-T brain scan were negative. Liver scan demonstrated multiple metastatic lesions. The patient was treated with Adriamycin[®], Cytosan[®], and Vincristine for 7 months, when she reached the maximum dose of Adriamycin. Thereafter, she received Cytosan and Methotrexate. Vincristine was discontinued after 9 months, due to fingertip paresthesias resulting in disability. She was judged to be in complete remission when her liver examination, scan, and chemistries returned to normal and her chest x-ray showed re-expansion of her collapsed right lower lobe. Her drug toxicity included moderate myelosuppression, nausea, vomiting, alopecia, and paresthesias.

Nine months after beginning treatment, she was re-admitted with a three-week history of increasing confusion and slow mentation. Within three hours she developed focal neurological deficits characterized by motor seizures on the right side, right hemiparesis, global aphasia, and irregular respirations. She was given intravenous Dilantin[®] and Valium[®]. Her blood pressure dropped to 70 mm Hg. systolic. She was infused with normal saline and given Decadron[®] 100 mg. intravenously. Three hours later she became normotensive. Urine specific gravity was 1.005. Lumbar puncture was negative including protein and cytology but a C-T brain scan demonstrated multiple lesions consistent with metastasis. The largest lesion occupied the suprasellar cistern (Fig. 1). Within 36 hours the patient's neurological status had improved and cranial irradiation was begun. On the second hospital day, polyuria and polydipsia were noted. A review of her intakes and

TABLE 1

WATER DEPRIVATION TEST			
Time	Weight (Lbs.)	Serum OSM. (mosm/kg)	Urine OSM. (mosm/kg)
0600	147.75	270	660
0700	—	—	464
0800	—	—	344
0900	—	—	230
1000	147.75	270	124
1100	—	281	92
1200	145.50	300	95
5u aqueous vasopressin	—	—	—
1300	—	—	165
1400	—	—	581
			% Increase
			U. OSM.
			after ADH
			73.7%

outputs demonstrated a 4-6 liter per day urine output. Over the next 24 hours, the patient averaged urine outputs of approximately 6 liters with an average intake of 5 to 6 liters. A water deprivation study (Table 1) and testing of pituitary function were undertaken (Table 2 and 3). She responded to parenteral Vasopressin but was refractory to Lysine Vasopressin given intranasally. She began therapy with DDAVP 0.1 ccs. B.I.D. intranasally which controlled her symptoms and kept her urine output below 2.5 liters a day. Urine specific gravity rose to 1.015. After the positive results of her anterior pituitary function studies, she was started on replacement therapy with Synthroid[®] and Cortisone. Her Decadron was tapered and discontinued. Her polyuria and polydipsia are well-controlled by synthetic DDAVP and she has resumed her normal activities.

RESULTS

Table 1 demonstrates the results of the Water Deprivation Study performed on the fourth hospital day. The protocol is adapted from Miller, et al, in 1970. (Note that in spite of seven hours of water deprivation, the high urine osmolality at the start was a result of previous aqueous Vasopressin given 12 hours prior to the initiation of the test.) Table 2 demonstrates the anterior pituitary function studies performed on this patient before provocation. Note that the L-Dopa growth hormone stimulation test was performed as a fasting test while the patient was still on Corticosteroids for reduction of cerebral edema. Table 3 demonstrates the TRH stimulation test.

DISCUSSION

Pituitary metastasis has been described at autopsy for a number of years. In 1914, Simmonds reported on the first case of distant pituitary metastasis leading to diabetes insipidus.³ Since then, numerous reports have described diabetes insipidus secondary to carcinoma. Hauck, in his 1970 series, reported a .95% incidence of diabetes insipidus in breast cancer patients and noted that 20% of the diabetes insipidus patients collected over 15 years had their disease secondary to a metastatic process.¹ The incidence of

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TABLE 2

A.B.—ANTERIOR PITUITARY FUNCTION STUDIES				
<i>T4</i> - 4.5 (RIA)	<i>T3 Uptake</i> - 43%	<i>FTI</i> 1.9	<i>TSH</i> - 0.3 uU/ML	<i>LH</i> - 2.4 mIU/ML (30-250 mIU/ML normal post-menopausal female)
<i>FSH</i> - 2.5 mIU/ML (50-200 mIU/ML normal post-menopausal female)			<i>Testosterone</i> - Less than 20 ng/100 ml (30-90 ng/100 ml)	
L-DOPA GROWTH HORMONE STIMULATION TEST				
<i>Min</i>	<i>gh Level</i>		<i>Normal Level</i>	
0	less than 1		less than 1-7	
30	less than 1		greater than 7	
60	less than 1		greater than 7	
90	less than 1		greater than 7	

TABLE 3

TRH STIMULATION TEST—500 ug TRH INTRAVENOUSLY		
<i>Min</i>	<i>TSH (uU/ML)</i>	<i>Prolactin ng/ml</i>
0	0.3	29.9 (32.5)
30	1.9	50.0
60	1.6	44.9
90	1.2	36.9

pituitary metastasis at autopsy from distant carcinoma is even higher than previously reported, ranging from 5.5% in Hauck's group of hypophysectomized breast carcinoma patients to 28% in Smulder's study of 71 patients in an autopsy series.⁴

The frequency of anterior pituitary involvement is rare. In Kovac's autopsy series, 18 pituitary metastasis were found in 1,857 cancer patients. Only four patients had anterior pituitary metastasis and none were symptomatic.⁵ In Teears' series of 88 cases, only 12 patients had metastatic disease limited to the anterior lobe, although frequently metastasis in the posterior lobe did have extension anteriorly.² Six of their patients had clinical diabetes insipidus, but only one had panhypopituitarism. Two recent case reports have documented anterior pituitary insufficiency from metastasis. Epstein reported an unusual case of ADH secreting oat-cell carcinoma of the lung which developed diabetes insipidus secondary to metastatic deposition, and had anterior pituitary insufficiency.⁶ Cox reported a case of symptomatic chiasmal compression, diabetes insipidus and anterior pituitary hypofunction from a metastatic breast lesion.⁷

Our patient presented with shock and confusion which responded to intravenous fluids and corticosteroids. When the patient improved, polyuria and polydipsia ensued. Subsequent questioning of the patient failed to reveal a previous history of polyuria and polydipsia. Because of the polyuria and C-T brain scan (see Figure 1), further provocative studies were undertaken. The Water Deprivation Study adapted from Miller, et al, 1970,⁸ performed on our patient, clearly demonstrated complete

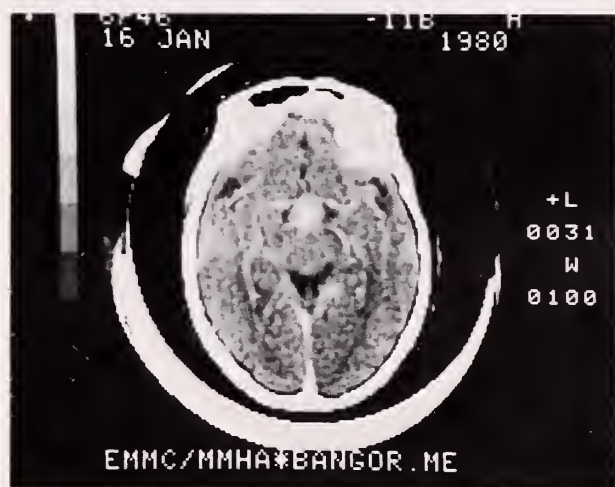


Fig. 1. A C-T brain scan with contrast enhancement demonstrates a large mass (the white circumscribed density) in the area of the suprasellar region.

diabetes insipidus. Lysine Vasopressin intranasally was ineffective, as is often the case, so she was placed on intranasal DDAVP with very effective results.

Her anterior pituitary was evaluated in several ways. In view of the low normal thyroid function studies and a low TSH (0.3 mU/ml), a TRH stimulation test was undertaken, measuring the TSH and prolactin response. Unfortunately, pharmacological dose of Dexamethasone used for cerebral edema can impair the TSH and prolactin response to TRH.¹⁰ However, the TSH response was much less than reported in patients on a similar high dose of Decadron and the prolactin response could be considered normal.

Growth hormone release can also be impaired by Dexamethasone administration.¹¹ This could be the case in this patient, but the complete lack of response implies anterior pituitary insufficiency. Finally, testosterone has recently been reported to be a sensitive screening test for panhypopituitarism in women.¹² In our patient, very low levels of testosterone were noted. Certainly, the LH and FSH levels were markedly diminished for a postmeno-

pausal patient, consistent with a serious gonadotrophin deficiency.

Tears, in his classic 1975 article, speculated that anterior lobe involvement by metastatic carcinoma was probably higher than reported, but was not diagnosed because of the near terminal state of many of these patients with diffuse metastatic disease. This certainly seemed to be the case in our patient, until control of her brain metastasis allowed further work-up. In fact, it is known that anterior pituitary insufficiency may ameliorate signs and symptoms of diabetes insipidus.¹³ Exogenous corticosteroids will tend to aggravate polyuria and may unmask occult diabetes insipidus. In our patient, aggressive therapy with steroids may well have brought to light clinical diabetes insipidus. The polyuria was the first sign suggesting further evaluation for pituitary metastasis.

Although anterior pituitary insufficiency secondary to metastatic disease is still considered rare, a greater awareness of metastatic pituitary disease may allow more frequent anterior pituitary detection by provocative studies. There is no question that there would still be a marked difference in the incidence of anterior pituitary and posterior pituitary metastases. Part of this can be explained anatomically because little, if any, systemic arterial blood directly reaches the anterior lobe.¹⁴ The hypothalamohypophyseal portal circulation of vessels arising from a capillary plexus in the median eminence is the major source of blood to the anterior region via the stalk. A secondary capillary supply from the lower stalk also feeds the anterior pituitary and this courses by way of the posterior lobe.¹⁴ In comparison, the posterior lobe has direct arterial circulation via the inferior hypophyseal artery. Because of the unique blood supply, it is tempting to postulate that large tumors could infarct the anterior lobe by direct extension into the stalk. Hauck, in his post-mortem series, could find no case that showed sufficient ischemia or infarction to explain anterior pituitary hormone deficiency.¹ Infarcts, if they were present, were tiny in nature and did not appear to be clinically significant.

Hypothalamic interruption due to metastatic disease may result in a significant decrease in anterior pituitary function. This would result in marked deficiency of the trophic hormones but an increase in prolactin. Our patient did have a similar picture but her TSH response to TRH was suboptimal and should be expected to increase normally with synthetic TRH if the anterior pituitary remained intact. As Snyder points out in his series of 100 patients with pituitary and hypothalamic disease tested with TRH, a subnormal TSH response to TRH in a patient with secondary hypothyroidism and a space occupying lesion strongly suggests pituitary involvement.¹⁵ Also, elevated prolactins do not necessarily imply hypothalamic involvement. It is difficult to distinguish pituitary from hypothalamic disease with elevated prolactins because intrasellar tumors may have elevated prolactins possibly related to pressure

phenomenon on the stalk itself rather than actual destruction.

In our case, a final anatomical analysis will await post-mortem studies. The case however, suggests what Tears speculated five years ago, that anterior pituitary involvement is probably more common than suspected. With the potential for complete replacement therapy and improved quality of life, correct anatomical diagnosis of pituitary hypofunction is imperative.

SUMMARY

A case of metastatic oat-cell carcinoma of the lung resulting in diabetes insipidus and clinical evidence of anterior pituitary hypofunction is reported. A review of previous studies is discussed and the importance of being aware of this clinical entity is stressed.

ADDENDUM

As of this writing, another case of diabetes insipidus was seen in our institution. This patient had anaplastic adenocarcinoma of the lung with multiple lymph nodes in the neck and polyuria. Water deprivation study demonstrated partial diabetes insipidus and a negative C-T brain scan was reported. Anterior pituitary function was completely within normal limits. The patient was treated with Chlorpropamide and Clofibrate (200 mg. of Chlorpropamide, 2 Gm. of Clofibrate) with moderate success for four weeks. He subsequently increased his urine output and is now being treated with intramuscular Vasopressin. DDAVP will be introduced into this patient within the next few days.

ACKNOWLEDGMENTS

The authors wish to acknowledge the assistance of Jody Burns, Nurse Practitioner, who worked intensely with A.B. both as an inpatient and as an out-patient, and B. Duffy, for manuscript preparation.

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Continued on Page 245

Eosinophilic Pleural Effusion in a Patient With Chronic Eosinophilic Pneumonia

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ABSTRACT

A case of histologically confirmed eosinophilic pneumonia with a significant pleural effusion is described. Thoracentesis and pleural biopsy demonstrated eosinophilic pleural inflammation. Although rarely described in this disorder, the presence of pleural fluid should not preclude the diagnosis of eosinophilic pneumonia and the finding of an eosinophilic pleuritis should suggest coexistent parenchymal eosinophilia.

INTRODUCTION

Chronic eosinophilic pneumonia was first described by Carrington, et al.¹ What is felt to be particularly distinctive of this disorder is the chest roentgenographic pattern of peripheral alveolar nonsegmental infiltrates. Pleural effusions associated with it are felt to be rare.² In fact, the literature describing this relationship is vague either in its characterization of the effusion or of the underlying parenchymal disorder.^{3,4,5,6,7} I recently treated a patient with biopsy proven eosinophilic pneumonia who also had a substantial pleural effusion which appears to be related to the underlying disorder.

CASE REPORT

A thirty-year-old white male was seen for complaints of left pleuritic chest pain, malaise, chills and fever. A chest x-ray was initially normal, but because of symptoms the patient was treated with erythromycin. Over the next two weeks penicillin and then tetracycline were subsequently given when clinical improvement did not ensue. Because of persistent pain, a repeat chest x-ray was taken which showed an infiltrate at the left base with a small pleural effusion. The patient was admitted to his local hospital where the WBC was 12,800 with 43 P, 4 B, 45 L, and 8 M but no eosinophils. Cold agglutinins were positive only at 1:8. The patient was retreated with erythromycin and clinically improved over the next week.

Readmission was prompted four days following discharge when right sided pleuritic pain and dyspnea occurred. A repeat chest x-ray showed a new right sided infiltrate in addition to the left sided abnormalities already noted. A repeat WBC was 11,800 with 59 P, 1 B 37L, and 3 E. A tine test was negative and a left sided thoracentesis was unsuccessful. The cold agglutinin titer had increased to 1:512 and, because mycoplasma pneumonia was considered the likely diagnosis, erythromycin was continued.

The patient again improved and two weeks following discharge his chest radiograph showed resolution of the right basilar infiltrate as well as improvement in the left sided infiltrate and effusion. Mild dyspnea continued, however, and after six weeks the patient's chest x-ray showed a new infiltrate on the right side along with a significant pleural effusion (Figure 1). He was then referred for further evaluation.

The physical examination was significant only for right sided chest dullness with decreased breath sounds. Laboratory data showed a hemoglobin of 16.2, WBC 12,200 with 13 percent



Fig. 1. Chest radiograph showing bilateral pulmonary infiltrates and a pleural effusion on the right.

eosinophils. The total eosinophil count was 1806. A sputum culture grew only normal flora and smears and cultures of sputum for AFB were negative. Serological titers for rheumatoid factor and antinuclear antibody were not elevated and a RAST battery was negative. A protein electrophoresis showed an elevated gamma fraction and an immunoelectrophoresis showed a mild increase in IgM. A convalescent phase titer for *M. pneumoniae* was positive at 1:128, but this was felt to be diagnostically inconclusive.

A thoracentesis of the right hemithorax revealed an exudate with a protein of 5.1 gm. and an LDH of 394. The white count was 2125 with 65 percent eosinophils and a pleural biopsy (Figure 2) showed inflammatory changes with eosinophilic infiltration of the pleura. A transbronchial biopsy (Figure 3) was then performed and showed eosinophilic infiltration of the alveolar walls and spaces. The patient was started on prednisone 80 mg. daily which was subsequently tapered. His radiographic abnormalities resolved promptly as did his symptomatic complaints, while his restrictive ventilatory defect showed marked improvement with FEV1 rising from 2.0 liters to 3.3 liters and FVC from 2.5 liters to 4.0 liters.

DISCUSSION

This patient's illness appears to satisfy the clinical, histologic and pathophysiologic features characteristic of chronic eosinophilic pneumonia.

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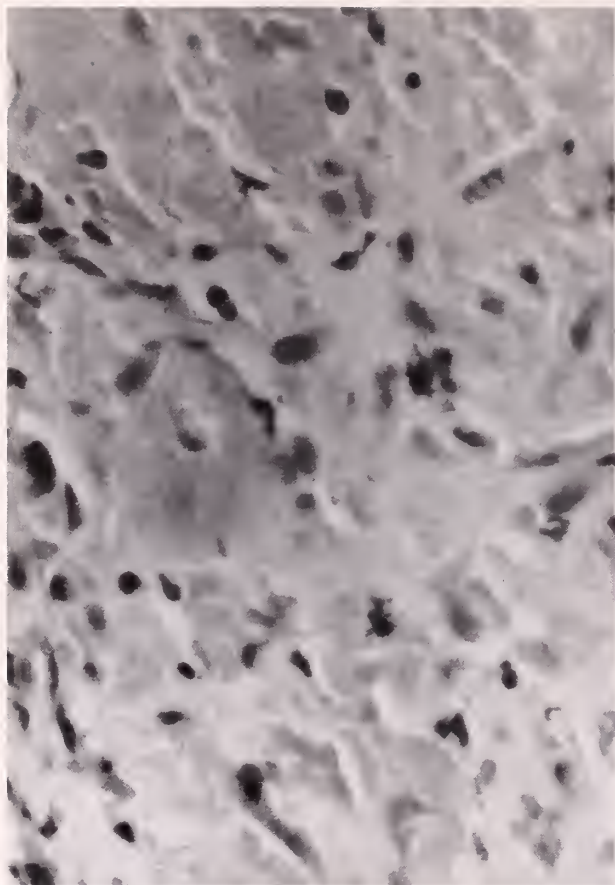


Fig. 2. Photomicrograph of a pleural biopsy showing an inflammatory exudate with eosinophils.

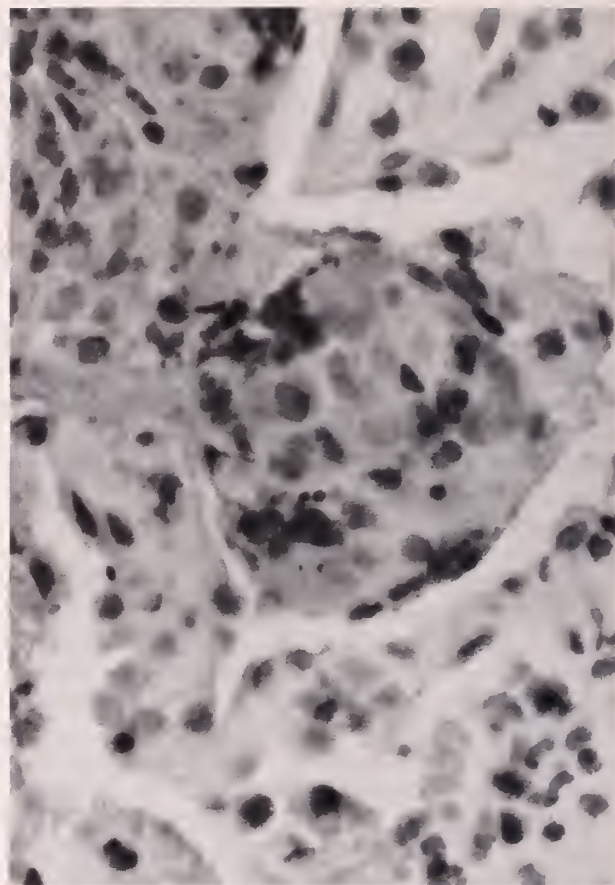


Fig. 3. Photomicrograph of a transbronchial biopsy showing thickened alveolar walls with numerous eosinophils.

Although the etiology is unknown a variety of drugs including penicillin have been implicated in the pathogenesis of this disorder.⁸ It is uncertain in this case whether the early course of his cold agglutinin positive pneumonia was due to *M. pneumoniae* since only a convalescent phase titer of indeterminate degree could be obtained. Cold agglutinins, however, have not been reported with chronic eosinophilic pneumonia. In view of the antibiotics, including penicillin, that the patient initially received, it is conceivable that the eosinophilic pneumonia may have been drug induced.

The radiographic characteristics of this disorder are so typical as to be considered virtually diagnostic. They are: 1) a peripheral infiltrative pattern described as the "photographic negative" of pulmonary edema, 2) prompt radiographic resolution with steroid therapy, and 3) recurrence of infiltrates in the same peripheral location with relapse. In view of the active inflammatory process that occurs adjacent to the visceral pleura, it is surprising that the presence of pleural fluid has only rarely been observed.

In the few literature reports in which pleural fluid was described with eosinophilic pulmonary infiltrates, the effusions were either poorly characterized or seemed to occur in conjunction with a severe systemic disorder with multiorgan involvement sug-

gestive of periarteritis nodosa.^{3,4,5,6,7} Eosinophilic pleural effusions while being relatively uncommon are not diagnostically specific.⁹ Eosinophilic infiltration of the pleura in eosinophilic pleural effusions, however, appears to be quite unusual. The exudative nature of this patient's effusion and the histologic demonstration of an eosinophilic pleuritis indicate that the pleural inflammation was directly related to the adjacent and underlying parenchymal disorder. Accordingly, the presence of an eosinophilic infiltrate of the pleura should suggest the possibility of coexistent pulmonary parenchymal eosinophilic infiltration as well. Finally, the radiographic demonstration of pleural fluid should not preclude the diagnosis of chronic eosinophilic pneumonia if the other usual criteria are present.

ACKNOWLEDGMENT

The author wishes to thank Dr. William G. B. Graham for reviewing this case report.

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DIFFERENTIAL DIAGNOSIS OF CHEST PAIN—With Known Coronary Heart Disease

Continued from Page 235

sympathetic dystrophy, was a frequent post-myocardial infarction complication in years past, sometimes protracted, painful and incapacitating, and probably led to the old warning against reaching over your head if you had "heart trouble." Since early mobilization, it has become rare.

Pain from upper gastrointestinal organs, especially esophagus, may be very difficult to differentiate from ischemic pain. Esophageal reflux pain at night may closely resemble nocturnal angina. See how it responds to treatment, if the situation permits the time, and remember that failure to demonstrate hiatus hernia or barium reflux by upper GI x-ray does not exclude the diagnosis. Esophageal spasm pain, less common, is frequently relieved by nitroglycerin, is most often related to emotional stress, and may be aggravated by swallowing, including cold liquids.

Patients I have known with demonstrated cause for both ischemic heart pain and for upper gastrointestinal pain, especially esophageal, often have difficulty in differentiating the pains, and when they apparently can, the description of either one may very much resemble ischemic pain.

Pain of psychogenic origin is not uncommon in patients with ischemic heart disease. It may be a chief complaint, obscuring or masking ischemic symptoms. Various anxiety syndromes with associated chest pain have been described. I think the hyperventilation syndrome, without evident or with over-looked frank breathlessness, is one of the commoner forms. Such patients may describe tightness of the chest and sense of difficult breathing that may easily be mistaken for ischemic pain.

Another syndrome of psychogenic pain, the "pain-prone patient," was described by Engel in 1956.² I

think this syndrome has been neglected. I would highly recommend reading his editorial "Pseudoangina" published in 1959.³ In addition to describing the syndrome, he describes an interview technique for these very suggestible patients that we can all use. He emphasizes that the subtle differential diagnosis between this syndrome and true angina pectoris depends on a carefully obtained history.

The patient's education should include how he can recognize his own ischemic pain and how he can differentiate it from other pains that he might have. For successful rehabilitation, the patient with stable or controlled angina, including post-coronary by-pass, and the post-myocardial infarction patient must understand this differential.

If a record of the nature of an individual's ischemic pain of the past is available when he later has pain for which he seeks help in the emergency room, it may be very valuable in helping decide whether there likely is an acute ischemic condition perhaps indicating hospital admission, even though the electrocardiogram may be normal, or a non-specific benign pain for which only reassurance is needed, even though the electrocardiogram is abnormal.

In conclusion, with so much that can be done for symptomatic coronary disease, medically and surgically, it is unfortunate if non-cardiac symptoms prevent return to as full a lifestyle as the cardiac condition permits.

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Acute Leukemia Masquerading as Polymyalgia Rheumatica

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ABSTRACT

A case of acute myelogenous leukemia which masqueraded as polymyalgia rheumatica or temporal arteritis for four months is presented. It is a reminder that polymyalgia rheumatica is a syndrome with a differential diagnosis, rather than a well defined disease.

INTRODUCTION

Polymyalgia rheumatica is characterized by proximal myalgias and muscle stiffness, a markedly elevated erythrocyte sedimentation rate, and, not infrequently, mild anemia and low grade fever, usually occurring in an elderly individual.¹ Weakness is secondary to pain and muscle atrophy is uncommon. Less frequent manifestations include abnormal liver function studies, carpal tunnel syndrome, and non-deforming synovitis of large joints. Indeed, there is evidence to suggest that a mild proximal large joint synovitis underlies the most prominent manifestations.² The etiology of the condition is unknown and more specific laboratory and pathological definition is lacking. The duration of the illness runs from months to years.³ Most cases respond to low doses of prednisone, though occasionally higher doses are required. On the other hand, some patients will respond to nonsteroidal anti-inflammatory medications.⁴ However, there are a number of better defined illnesses which may present in exactly the same fashion.^{5,6} Therefore, it is important to be occasionally reminded that polymyalgia rheumatica should be approached as a syndrome with a differential diagnosis and not a specific disease entity, the presumptive diagnosis of which eliminates other possibilities.

CASE REPORT

A 74-year-old woman was hospitalized in June 1979 with a one-month history of fever to 102°F, weight loss of fourteen pounds, proximal myalgias, and anorexia. A marked decrease of visual acuity in her right eye prompted an ophthalmologic examination but the only abnormality noted was senile macular degeneration, stable since 1975. She had a 40-year history of seasonal asthma and cigarette-related chronic obstructive pulmonary disease requiring frequent treatment with various bronchodilators, tranquilizers and short courses of prednisone. Her hematocrit in 1976 was 46 percent. Her physical examination was normal except for obesity and a fever of 101°F. Laboratory studies revealed a hematocrit of 36 percent, white blood cell count 7400/mm³ (80 neutrophils, 15 lymphocytes, and 5 monocytes), normal platelets on blood smear, normal urinalysis, normal SMA-18 (except for a lactic dehydrogenase of 230), but the erythrocyte sedimentation rate was 137 mm/hr (Westergren method). Blood cultures were negative. An intravenous pyelogram and chest x-ray were not helpful. She

became afebrile after 48 hours and was discharged. In August, as an outpatient, her fever recurred and she was given Erythromycin® 250 mg. q.i.d. Temperatures waxed and waned. When her weight fell another six pounds she was admitted to the hospital for the second time. Her temperature was 100.5°F and diminished breath sounds with a few scattered wheezes were noted on chest auscultation. Laboratory studies revealed a hematocrit of 27 percent. Stool guaiacs and bleeding and clotting parameters were normal. The erythrocyte sedimentation rate was greater than 150 mm/hr. Other studies repeated from her first admission were unchanged. Thyroid function tests and quantitative immunoglobulins were normal. Anti-nuclear antibody and rheumatoid factor were not present. A serum protein electrophoresis exhibited a nonspecific elevation of alpha-1, alpha-2 and beta fractions. Multiple blood cultures and febrile agglutinins were normal. X-ray studies included a gallbladder series, barium enema, upper gastrointestinal series and metastatic survey. These and liver and gallium scans were not helpful. Bone marrow and liver biopsies and cultures were normal. No diagnosis was evident after these studies and oncology and infectious disease consultations. She did not respond to penicillin and streptomycin therapy. A rheumatologist considered temporal arteritis or other necrotizing vasculitis to be more likely than polymyalgia rheumatica because of the history of sudden visual loss, fever, and marked anemia. However, bilateral temporal artery and skin and muscle biopsies were normal. A presumptive diagnosis of polymyalgia rheumatica was made and prednisone 15 mg. per day was initiated. She did not respond, but when the dose was increased to 60 mg. per day her fever remitted, myalgias diminished, and she was discharged. In September, she was admitted for the third time with fever attributed to right lower lobe pneumonia and oral candidiasis. The hematocrit was 29 percent, white blood cells 9900/mm³ (37 neutrophils, 8 bands, 34 lymphocytes, 6 metamyelocytes), and erythrocyte sedimentation rate 105 mm/hr. Sputum culture revealed mixed oral flora. Fever, cough, and right lower lobe infiltrate responded to antibiotics and respiratory care. Prednisone 60 mg. per day was continued and the patient was discharged. The abnormal white cell differential was attributed to corticosteroid therapy and infection. In October, fever to 103°F and increasing dyspnea led to her final admission. The chest x-ray was stable. The hematocrit was 26 percent, white blood cells 3800/mm³ (with 6 promyelocytes and 4 blast forms), and platelet count 95,000/mm³. A repeat bone marrow examination confirmed the diagnosis of acute myelogenous leukemia. She later died at home; an autopsy was not permitted.

COMMENT

The presumptive diagnosis of polymyalgia rheumatica was based on the markedly increased erythrocyte sedimentation rate, proximal myalgias, and age of the patient (fever and anemia were considered secondary features). Other examinations had failed to support infectious, malignant or vasculitic etiologies. The history of visual decrement was three months old, there had been no further neurological or ophthalmological disturbance, and bilateral temporal artery biopsies were negative. When the patient did not respond to low dose prednisone therapy, temporal arteritis (presumptively missed by biopsy) was reconsidered and the patient initially seemed to respond to higher doses of corticosteroids. Her relapse indicated the need for reevaluation, during which acute myelogenous leukemia was diagnosed.

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DISCUSSION

When an elderly patient presents with proximal myalgias or stiffness and an elevated sedimentation rate the differential diagnosis listed in Table 1 should be considered. Besides a complete history and physical, the laboratory evaluation should include those studies listed in Table 2. Further studies are dependent upon any abnormalities found in the screening evaluation, physician philosophy, and patient follow-up. As examples: marked anemia warrants a bone marrow examination; the question of whether the temporal artery biopsy is indicated in all patients presenting with polymyalgia rheumatica remains moot;⁷ and a poor response to appropriate therapy warrants a reevaluation. If a temporal artery biopsy is not performed routinely, then any suggestion of temporal arteritis such as headaches, eye pain, visual disturbance, throat pain or lingual angina, marked anemia or high fever, or scalp tenderness should prompt the examination. On the other hand, if the patient does not respond to 10 or 15 mg. of prednisone, then an evaluation for malignancy, and various biopsies for temporal arteritis and other types of vasculitis should ensue.

In summary, we are reminded that polymyalgia rheumatica is but a syndrome: though the initial evaluation is straightforward, there is a differential diagnosis to be considered, and the "specific illness" is diagnosed by exclusion. A lack of response to the usual therapy requires a reassessment of the diagnosis.

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TABLE 1

POLYMYALGIA RHEUMATICA SYNDROME DIFFERENTIAL DIAGNOSIS*
Polymyalgia Rheumatica
Temporal Arteritis (and other necrotizing vasculitis)
Rheumatoid Arthritis, Dermatomyositis (and other connective tissue diseases)
Multiple Myeloma (and other occult malignancies)
Subacute Bacterial Endocarditis, Tuberculosis (and other occult infections)

*Diseases such as osteoarthritis, cervical spondylosis, hyper and hypothyroidism, Parkinson's disease, depression and fibrositis syndrome may exhibit similar clinical features but characteristically have normal erythrocyte sedimentation rates.

TABLE 2

POLYMYALGIA RHEUMATICA SYNDROME INITIAL LABORATORY EVALUATION*
Complete Blood Count
Erythrocyte Sedimentation Rate
Urinalysis
Chemistry Profile (including Blood Urea Nitrogen, Calcium, Alkaline Phosphatase and Creatinine Phosphokinase)
Stool Guaiac
Protein Electrophoresis
Rheumatoid Factor
Antinuclear Antibody
Chest X-ray

*Remember that patients with polymyalgia rheumatica may exhibit abnormalities of liver function tests and that elderly patients may exhibit positive latex fixations and antinuclear antibody studies.

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PITUITARY METASTATIC DISEASE: Report of a Case and Review of the Literature

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Diagnostic Imperatives In Internal Medicine

The Timely Detection of Treatable Disease

Pulmonary Diseases

BARRY L. FANBURG, M.D.*

Many pulmonary diseases occur insidiously and never precipitate a crucial diagnostic moment. Some, such as pneumonias and lung tumors, do require early and accurate diagnosis but are discussed elsewhere. Others, such as massive hemoptysis or acute upper airway obstruction, are dramatic enough to be regarded as medical emergencies and are outside the scope of this paper. Still other pulmonary disorders are neither catastrophic nor indolent but, if unnoticed or unattended, can harm or kill the patient; they are the conditions to be discussed.

The lungs' repertoire of symptoms is relatively limited, but analyzed in conjunction with history, physical findings, and laboratory studies, can give a great deal of specific information.

Dyspnea

Shortness of breath is frequently the first symptom of many lung diseases or of heart failure; occasionally it reflects other problems, such as generalized weakness, obesity, or psychological disturbance (Table 1). Although the term "shortness of breath" or some equivalent is likely to be used in all these circumstances, the actual manner of presentation can be distinctive of a particular disorder.

For example, dyspnea begins very gradually in patients with chronic obstructive airway disease; for months or years they may only recognize it as a slight limitation in their capacity for exertion. Then, at some point, they identify the symptom as a persistent difficulty in catching their breath and often are able to specify the amount of effort that brings it on. *Asthma* produces an episodic dyspnea, which may begin when the patient is at rest and in any case is not necessarily related to expenditure of effort. Obstruction of the *upper* airway may also cause dyspnea but is usually acute and has an obvious cause. More subtle evolution also occurs, however, as in the case of laryngeal stenosis after an endotracheal tube has been removed, when a goiter is substernal, or with compression of the trachea by tumor, and such causes may go unrecognized.

These three obstructive causes of dyspnea are also associated with distinctive physical findings. Chronic obstructive airway disease, affecting the lower airway, is associated with decreased breath sounds, at least, and some hyperresonance to percussion. Normal breath sounds imply that some other diagnosis is

a cause of the dyspnea and should prompt a further search. Upper airway obstruction also is associated with a distinctive physical finding: inspiratory stridor which sometimes can only be heard at the base of the neck near the sternal notch. Asthma, on the other hand, because it is intermittent, may yield relatively normal physical findings between attacks.

Whereas x-rays are of little help in the diagnosis of early chronic obstructive airway disease, the condition is readily recognized when expiratory air flow is measured during pulmonary-function studies. In more advanced disease, of course, hyperaeration and lowering of the diaphragm becomes apparent on x-ray. When the upper airway is occluded, tomography of the larynx and trachea may be quite helpful. The inspiratory flow pattern, which can be measured with a special apparatus for flow-volume analysis, may provide the first indication of upper airway obstruction and permits the severity of the condition to be assessed. In asthma, x-rays are likely to be uninformative unless a secondary process, such as infection, is complicating the disease, and pulmonary-function studies may or may not show the abnormality because of the intermittancy of airway obstruction.

Diseases affecting the lung's *parenchyma* may cause shortness of breath even at rest, but certain conditions, including sarcoidosis and some occupational diseases, seem extensive on x-rays and yet produce relatively little in the way of symptoms. Occasionally the reverse is true: dyspnea is significant but x-ray findings are minimal, as may be the case with scleroderma or cancer spreading through the lymphatics. The severity of dyspnea is, no doubt, a function of the histological location of the disease process and its effect on gas exchange. Physical findings in parenchymal lung disease may be quite variable. Râles are common, or there may be signs of consolidation, but in the presence of significant disease the chest examination can occasionally be perfectly normal, as it often is with sarcoidosis. Chest x-rays help to distinguish between diffuse infiltration of the alveolar spaces and diseases confined to the interstitium. "Alveolar filling" is the radiological term for a pattern of small, rounded air pockets delimited by densities; this picture indicates that an exudate, transudate, or hemorrhage is filling alveolar spaces. An "air bronchogram" indicates that there is inflammation in alveoli surrounding the bronchi. Increased interstitial markings, on the other hand, correspond to exudate, transudate, or fibrosis in the interstitial

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TABLE I

MAJOR CAUSES OF SHORTNESS OF BREATH

	<i>Presentation</i>	<i>Specific Physical Findings</i>	<i>Chest X-ray Findings</i>	<i>Pulmonary Function Studies</i>
A. Airway disease				
1. Chronic obstructive pulmonary disease	Insidious Exertional dyspnea	Generalized decrease in breath sounds and hyperresonance to percussion	Hyperaeration	↑ residual volume ↓ vital capacity ↓ air flow
2. Asthma	Episodic dyspnea	Expiratory wheezes	± Hyperaeration	Same as (1)
3. Upper airways obstruction	Acute or insidious dyspnea	Inspiratory stridor	Upper airway occlusion	↓ inspiratory air flow
B. Lung parenchymal disease				
1. Infiltrate				
a. Generalized (such as "non-cardiac" pulmonary edema)	Acute dyspnea	Generalized râles	"Alveolar flooding"	↓ vital capacity
b. Limited (such as pneumonia)	Acute dyspnea	Localized râles	"Air bronchogram"	↓ vital capacity
2. Interstitial process	May be insidious as with fibrosis Exertional dyspnea	"Crackles" at posterior bases of lungs	"Interstitial markings"	↓ vital capacity Possible decrease in diffusion
C. Pleural disease				
1. Infectious pleurisy	Acute onset May be associated with pain	Possible pleural friction rub	Pleural effusion	↓ vital capacity
2. Other pleurisy	Variable onset May be associated with pain	As above	As above	As above
3. Pneumothorax	Often acute and at rest	Decreased breath sounds	Pneumothorax	↓ vital capacity
D. Pulmonary vascular disease				
1. Pulmonary embolus	Acute onset usually	Variable	Variable	Variable
2. Pulmonary hypertension	Gradual onset	Variable	Enlarged pulmonary artery	Variable Possible decrease in diffusion
E. Non-pulmonary causes				
1. Congestive heart failure	Acute or insidious onset	Basilar râles	Generalized ↑ markings	Variable
2. Obesity	Insidious onset	Obesity	Non-specific	↓ vital capacity
3. Poor conditioning	Insidious onset	None	None	Exercise intolerance
4. Psychogenic	Inability to take a deep enough breath at rest	Demonstration of breathing pattern	None	Normal

spaces. These various x-ray findings help to support the diagnosis of an infiltrative process, but they give no specific information as to the histological lesion and its etiology. The measurement of lung volumes and/or diffusing capacity may help to quantitate the extent of alveolar, interstitial or vascular disease, but pulmonary function studies do not, in general, help in distinguishing these conditions.

Pleural disease can cause shortness of breath either abruptly or gradually. The dyspnea of infectious pleurisy is usually quite sudden in onset and often persists even during rest. Tumor or fluid retention lead to a more gradual onset, both of the pleural ef-

fusion and its associated dyspnea. Because pain is associated with breathing, the patient may have difficulty distinguishing between it and true shortness of breath. Physical examination is usually helpful in cases of pleuritic disease; the examiner hears dullness to percussion or a pleural rub. And the condition is nearly always obvious on x-rays, although a small effusion or pneumothorax may require decubitus views before it is seen.

Pulmonary vascular disease often announces itself with dyspnea. Shortness of breath while at rest may occur suddenly with acute pulmonary embolism or more gradually as recurrent small emboli com-

promise the vasculature. Pulmonary hypertension, whether primary or as a feature of interstitial disease, produces exertional dyspnea; in part, this may be due to a decrease in cardiac output resulting from the high vascular resistance. Whatever the cause of pulmonary vascular disease, chest findings are usually unremarkable, but a louder-than-normal sound from the closing pulmonary valve or a right ventricular lift may be clues to its presence. Routine x-ray examination may contribute little more to the diagnosis unless there is enlargement of the central arteries—a clue to pulmonary embolism in the appropriate setting or to pulmonary hypertension.

Of course, shortness of breath may be a symptom of *nonpulmonary* disease. Congestive heart failure is the most obvious and most common. Severe anemia may also be first perceived by the patient as exertional dyspnea. Obesity or poor physical condition can lead to shortness of breath when physical effort is called for. Any psychological distress sometimes is manifested as a sense that the patient cannot “get a deep enough breath” while at rest. A complete examination usually reveals these causes of dyspnea. Exercise studies can help to document the symptom of dyspnea on exertion and may be useful in distinguishing cardiac or pulmonary disease from “poor conditioning.” Shortness of breath should never be attributed to obesity, poor physical condition, or psychological disturbance, however, unless other causes have been excluded.

Hemoptysis

Hemoptysis of any degree must be pursued because (1) it may signal the presence of a tumor or other lesion that should be resected, or (2) it may presage a subsequent, massive hemorrhage. Although hemoptysis has a number of causes (Table 2), patients commonly believe that it means cancer and, therefore, are especially likely to be anxious about it.

Information from the history may be suggestive of a diagnosis, as when the patient reports a chronic cough, cigarette smoking, or previous hemoptysis, but it is not diagnostic. Hemoptysis can be mistaken for nasal, oropharyngeal, or sometimes even gastrointestinal bleeding—both by patient and physician. It is always useful, moreover, to have the patient save the specimen so that an extensive work-up can be avoided if the substance in question proves not to be blood. If sputum is produced as well as blood, a specimen should be saved and examined for tumor cells, acid-fast or other bacteria, or hemosiderin-laden macrophages (which point to alveolar hemorrhage).

Unless there is evidence for metastatic cancer, for example a palpable lymphadenopathy, physical examination may be as unhelpful as the history in narrowing the diagnosis. A chest x-ray, however, can point the way. Evidence of infiltrative disease in the presence of fever suggests infection. An infiltrate that clears rapidly may reflect hemorrhage of the sort that occurs with vasculitis. A mass is probably a tumor.

TABLE 2

CAUSES OF HEMOPTYSIS	
I.	<i>Inflammation</i>
	A. Bronchitis
	B. Bronchiectasis
II.	<i>Infection</i>
	A. Bacterial
	B. Fungal
	C. Mycobacterial
III.	<i>Tumor</i>
	A. Bronchogenic Ca
	B. Bronchial adenoma
IV.	<i>Vascular</i>
	A. Pulmonary embolus
	B. Vasculitis
V.	<i>Other and unusual</i>
	A. Anticoagulation
	B. Sequestration
	C. Endometriosis
	D. Contusion
	E. Nasal, oropharyngeal and gastrointestinal bleeding

If the diagnosis is still uncertain, fiberoptic bronchoscopy is the next step and should be performed as soon after the acute bleed as possible; for the bronchus from which the blood originates may be identified and even small lesions located. Profuse bleeding, on the other hand, may obscure its own source.

If bronchiectasis is a possible cause, the bronchoscopy should probably be planned so that bronchography can be done at the same time. Patients with chronic bronchitis or bronchiectasis may suffer hemoptysis recurrently and sometimes profusely. It is neither practical nor particularly useful to work them up each time, but they should be followed with chest x-rays to rule out the appearance of a new lesion. Further work-up should be guided by circumstances.

Modest hemoptysis often accompanies bacterial pneumonias, but it is altogether rare in viral pneumonias. On the other hand, lung abscess or an infected sequestration can lead to considerable bleeding. An arteriogram may prove that a sequestration is the source by showing that its blood supply comes from the aorta. Mycobacterial infections as well as mycoses or other infections in the form of a mycetoma, can erode large vessels to cause profuse hemorrhage.

Bronchogenic tumors, which will be discussed later, may announce themselves with hemoptysis, even before they are visible on x-ray; in such cases, bronchoscopy provides the first evidence of a lesion. Pulmonary embolism may at times cause hemoptysis, probably as a consequence of infarction. Wegener's granulomatosis and Goodpasture's syndrome, among other forms of vasculitis, may also present with hemoptysis.

Anticoagulants in themselves predispose a patient to hemoptysis, and when they are given to treat pulmonary embolism bleeding may be caused either by recurrent disease or by the treatment. Determining

TABLE 3

SLEEP APNEA

<i>Central</i>	<i>Causes</i>		<i>Manifestations</i>
	<i>Obstruction</i>		
Bulbar poliomyelitis	Obesity (Pickwickian Syndrome)		Daytime sleepiness and nocturnal insomnia
Brainstem infection	Adenotonsillar enlargement		Noisy snoring
Brainstem neoplasm	Acromegaly		Marked movement during sleep
Cervical cordotomy	Macrognathia		Intellectual and personality changes
Spinal surgery	Temperomandibular or joint disease		Sexual impotence
Primary hypoventilation	Myotonic dystrophy		Pulmonary or systemic hypertension
			Polycythemia
			Unexplained nocturnal death

which it is can be quite difficult. Anticoagulation may also precipitate bleeding from an endobronchial lesion; in some cases, then, bronchoscopy is needed to pursue the diagnosis.

Pulmonary endometriosis is a rare cause of hemoptysis, but it should be considered when episodes recur at monthly intervals.

Profuse hemoptysis is often very difficult to treat. Inducing embolism of the pulmonary vasculature is not demonstrably effective, and surgical excision may, therefore, be required. If cough exacerbates the hemorrhage, limiting it with opiates may be indicated.

Cough

Cough is a common finding in pulmonary disease, and the reason for it is often not obvious. After an infection, coughing can persist for weeks or months and may become quite worrisome to patients. Coughing may also be a prominent feature of asthma. When no clear cause for a cough can be established by a preliminary work-up, a reasonable course is to follow the patient for 3 or 4 weeks and then, if there is no improvement, to perform bronchoscopy.

Isolated X-ray Abnormality

In the absence of other symptoms, a patient may be seen because an abnormality has appeared on a chest film obtained for some reason other than pulmonary disease. Usually, in this circumstance, the diagnosis will prove to be lung tumor, sarcoidosis, or another interstitial disease of some sort.

Disturbances in the Control of Ventilation

Disturbances in the control of ventilation can manifest themselves in misleading ways. For example, patients who hyperventilate may bring themselves to unconsciousness, in which case the differential diagnosis includes all the other causes of "fainting." Similarly, patients who have apneic episodes during sleep (so-called "sleep apnea") may first be observed to exhibit a personality disorder, which presumably results from sleep deprivation. Sleep apnea may be caused either by neurologic dysfunction or by a chronic partial obstruction of the airway

(Table 3). In the latter case, profound snoring during sleep may be the tip-off. Diagnosis requires that the patient's ventilation, chest-wall movement, and arterial oxygen saturation be monitored during sleep. Treatment of the condition is directed at its cause.

Airway Obstruction

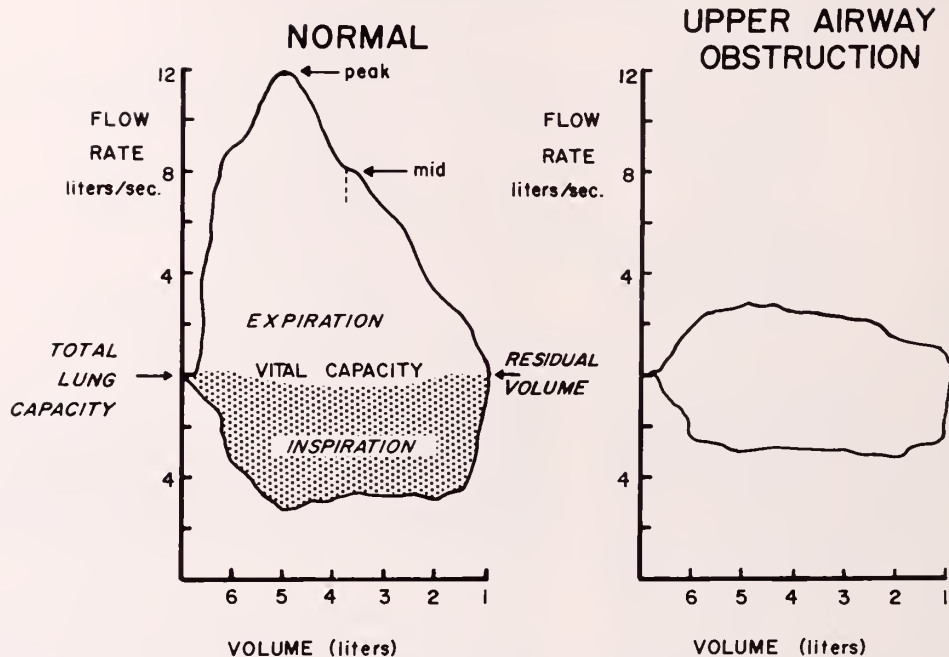
It is often obvious when the upper airway is obstructed acutely: onset is sudden, there is a loud inspiratory stridor, and accentuated movement of the chest wall can be observed. These findings may occur after aspiration of food. But even in an acute episode, after the first few moments, the diagnosis may be elusive. As the patient becomes cyanotic and unresponsive, a heart attack may seem the more likely process. When acute aspiration is recognized, it should be treated first with back-slapping or the Heimlich maneuver; if this approach fails, and an impacted particle is probably the cause of obstruction, an emergency tracheotomy may save the patient's life. Likewise, in laryngospasm caused by an acute allergic reaction, tracheotomy may be necessary if epinephrine is ineffective.

Obstruction that has gradually developed in the upper airway does not necessarily broadcast its presence with loud stridor. The presenting symptom of an insidious process may be dyspnea on exertion. A history of tracheal intubation may be the clue to stenosis; tumors, infections, thyroid enlargement, and bilateral paralysis of the vocal cords are other possible causes.

The diagnosis should be pursued by methods to visualize the obstruction: direct or indirect laryngoscopy, bronchoscopy, x-ray tomography. Pulmonary function study, including air-flow and lung-volume measurements for a "flow-volume" analysis (Figure 1), may be immensely helpful in detecting a fixed obstruction. It also indicates the functional extent of the obstruction and the patient's response to treatment. Therapy is directed to the particular cause of obstruction, but in some cases, temporary or permanent tracheostomy may be required.

Chronic obstructive lung disease has been discussed. The process itself is irreversible, but it can be arrested if smoking is discontinued, and symptomatic relief is afforded by bronchodilators and oxygen

FLOW-VOLUME ANALYSIS



A. Recording of normal flow and volume changes during exhalation and inhalation.

B. Recording of flow and volume changes of patient with upper airway obstruction. Note the flatness of the inspiratory limb of the tracing and the decreased expiratory flow.

therapy, which improve arterial oxygenation and inhibit the development of progression of pulmonary hypertension. If the disease is detected in the second to fourth decade of life, or if there is a strong family history for it, serum levels of alpha-1-antitrypsin should be measured; if a deficiency is found, there is added incentive to stop smoking and the information may also be useful for genetic counseling.

The diagnostic challenge of *asthma* is not usually in recognizing the disease but rather in assessing its severity. It is possible for a patient in whom wheezing is minimal and arterial CO_2 pressure (PaCO_2) is normal to be dreadfully ill, and yet the normal findings lull the physician into a false sense of security. This situation arises when the obstruction has become so severe that many airways are blocked and thus simply incapable of wheezing. The PaCO_2 , which should be low as a result of the patient's ventilatory efforts, begins to rise as respiratory failure approaches. Instead of relaxing his vigilance, the physician should be approaching this patient with vigorous therapy, including not only xanthine derivatives, sympathomimetics and steroids, but possibly also consideration for endotracheal intubation.

Acute episodes of "asthma" or late onset of the condition, may be precipitated by a variety of allergens, both natural and industrial. The conditions sometimes have names with an exotic or old-fashioned aura: bird fancier's disease (from bird excreta), farmer's lung (from molds), silo filler's disease (caused by oxides of nitrogen). But the phenomenon also affects plastic workers, for exam-

ple, exposed to hydrocarbons in the course of their work. History usually guides the diagnosis, and once it is made, treatment, obviously, is to avoid the provocative agent.

Atelectasis

Atelectasis should be anticipated in a postoperative patient. It also appears in patients with limited mobility of the chest wall owing to pain or binding of the chest. Anyone who has difficulty with the control of swallowing is also susceptible. Dyspnea is usually the first indication of significant atelectasis, but the report of a decreased arterial oxygen pressure may be the first warning in a hospitalized patient. Chest x-ray usually demonstrates the abnormality. Therapy begins with chest percussion to dislodge a mucus plug. Failing that, fiberoptic bronchoscopy under local anesthesia is the next step.

Lung Tumors

The small, solitary nodule, measuring 1 to 2 cm in diameter on a chest film, is one of the most serious of diagnostic challenges. Tumors detected at this stage can be resected with a relatively high rate of cure (but screening programs to find these lesions do not seem worth the yield, except perhaps in high-risk groups). Once detected, the solitary lesion poses two questions: (1) Is it cancerous? and (2) If so, has there been metastasis? The first often cannot be answered before surgery. Although cytological examination of sputum, bronchial washes, or bronchial brushings may establish that the lesion is malignant, negative results leave the matter in doubt. And although there

TABLE 4

PARANEOPLASTIC SYNDROMES ASSOCIATED WITH LUNG CANCER

- A. Endocrinopathies
 - 1. Gynecomastia
 - 2. Cushing's syndrome
 - 3. Inappropriate anti-diuretic hormone secretion
 - 4. Parathyroid hormone secreting tumor and hypercalcemia
 - 5. Carcinoid syndrome
- B. Neuromuscular disorders
 - 1. Myasthenic syndrome
 - 2. Peripheral neuropathy
 - 3. Cerebellar degeneration
- C. Connective tissue disorders
 - 1. Clubbing of nailbeds
 - 2. Pulmonary hypertrophic osteoarthropathy
 - 3. Dermatomyositis
 - 4. Acanthosis nigricans
- D. Vascular disorders
 - 1. Thrombophlebitis
 - 2. Thrombocytopenia
 - 3. Thrombocythemia

is difference of opinion about when to operate, resection is usually advisable. Delay is, as a rule, warranted only if (1) the patient is a poor surgical risk, (2) the lesion has not grown for a year or two, as shown by earlier x-rays, or (3) the lesion is diffusely calcified. A history of exposure to fungus or tuberculosis is insufficient to justify delay; neither condition eliminates the possibility that cancer is present.

The question of metastatic disease may be more difficult to assess. Mediastinoscopy and computerized tomography of the chest and mediastinum may be helpful, but their full utility in detecting metastases has not been firmly established. Sometimes, a paraneoplastic syndrome is the first indication of a lung cancer, and treatment of the tumor relieves the patient of his endocrine or other symptoms (Table 4).

A pleural effusion may announce the presence of tumor even when there are no pleural metastases. One such circumstance is Meigs's syndrome, in which fibromas or fibroma-like tumors of the ovary are associated with peritoneal or pleural effusions. With removal of the tumor, the pleural fluid often disappears.

Pulmonary Infections

Although this subject is more extensively discussed elsewhere, a few points bear emphasis here.

Patients with chronic obstructive pulmonary disease are highly susceptible to pneumonia and likely to deteriorate very rapidly once they have it. They should receive antibiotics early, as well as good physical therapy and careful attention to clearing of secretions. Oxygen may be required, but it must be administered cautiously because the patient's ventilatory drive, in the presence of chronic CO₂ retention, may depend upon persisting hypoxemia. A flow rate of oxygen of 2 to 4 liters a minute is usually as much as is advisable.

The objective of early therapy is to prevent intuba-

tion, but one of the following conditions may require use of a ventilator: (1) acute rise in PaCO₂ with a significant decrease in pH, (2) severe hypoxemia not corrected by enriching the inspired atmosphere, or (3) serious difficulty with clearing secretions.

Suspected opportunistic infections of the lung may require bronchial brushings and lung biopsy done either by fiberoptic bronchoscopy or by an open procedure. Although open biopsy of the lung offers a higher potential yield of diagnoses, bronchoscopy with brushings or transbronchial biopsy is far easier and safer.

Pulmonary Edema

Although the cause of cardiogenic pulmonary edema is usually obvious, the other etiologies of pulmonary edema may be less easily spotted. Pulmonary edema is sometimes seen in people suddenly exposed to very high altitudes. It can be a complication of cerebral trauma or cerebrovascular accident, of uremia, or of heroin abuse. Ingestion of a toxic substance, such as paraquat, may cause pulmonary edema, and, of course, it can be caused by aspiration. In general, the physical findings resemble those of the cardiac syndrome, although venous pressure is often normal and the heart not enlarged. Water in the alveolar and interstitial spaces becomes audible as râles and visible as the "alveolar" pattern on x-ray. Treatment resembles that of pulmonary edema in general, with diuretics as the mainstay.

Interstitial Lung Disease

There is considerable confusion about the definition of interstitial lung disease and about its classification. Interstitial lung disease refers to an inflammatory or a fibrotic process in the interstitium. However, there is a belief that at least some of the interstitial diseases (such as "desquamative pneumonia") may actually begin in alveolar spaces. Most of the entities referred to as interstitial disease, including forms of interstitial fibrosis, interstitial pneumonias, and sarcoidosis, do not have identifiable etiologic agents. Some do, however, respond to therapy such as with steroids or with immunosuppressive agents and, therefore, may be considered diagnostic imperatives.

Desquamative interstitial pneumonia may be an early stage of interstitial pneumonias of unknown etiology. It should be considered in a patient who presents with dyspnea, low-grade fever, and bilateral infiltrates on chest x-ray. Biopsy is needed for the diagnosis; it shows mononuclear infiltrates and proliferation of cells into the alveoli. Steroid therapy often produces a remission, but may be required for several months or longer. Steroids may also be effective with some of the other more "usual" interstitial pneumonias, which show a pattern of fibrosis and inflammation.

Although I have emphasized that sarcoidosis may present with a minimum of symptoms, it can also produce an acute picture (Loeffgren's Syndrome) of fever, arthritis, and erythema nodosum; pulmonary

TABLE 5

SOME CAUSES OF ADULT RESPIRATORY DISTRESS SYNDROME

Cause	Example
1. Shock	Traumatic hemorrhage, burns, pancreatitis
2. Infection	Viral pneumonias, gram negative pneumonia
3. Aspiration	Comatose patient, gastric tube feeding, drowning
4. Radiotherapy	Radiation pneumonia
5. Ingestion	Paraquat
6. Inhalation	Chlorine, sulfuric acid, smoke inhalation
7. Pulmonary vascular occlusion	Intravascular coagulation, fat emboli

manifestations include inflammation or fibrosis with the attending symptoms. Steroids usually produce a remission, but recurrence is possible when therapy is stopped.

Acute Respiratory Failure

Acute respiratory failure, often referred to as the adult respiratory distress syndrome when there is associated parenchymal lung disease, may result from many causes, some of which have already been discussed. A listing of possible causes of the respiratory distress syndrome is included in Table 5. In these cases there is rapid development of arterial hypoxemia, at times with associated hypercapnia. The hypoxemia results from a combination of ventilation-perfusion mismatching, diffusing defects, and intrapulmonary arteriovenous shunting. Hypercapnia occurs secondary to impairment of mechanics of ventilation and, in itself, is a cause for hypoxemia through alterations in alveolar gas composition. The patient usually has tachypnea. The clinical features that may accompany the blood gas alterations are noted in Table 6. The measurement and close follow-up of arterial blood gases are critical for management. Oxygenation may at times be maintained adequately by nasal and oropharyngeal delivery systems, but often requires intubation when these systems do not suffice or when mechanical failure is sufficient to result in worsening hypercapnia and acidosis. These patients frequently need artificial ventilation. A discussion of this modality of treatment is beyond the scope of this paper.

Pulmonary Vascular Disease

The manifestations of pulmonary embolism have already been discussed. The challenge of this diagnosis is, in large part, the difficulty of ruling it out, and yet one is reluctant to subject a patient to anticoagulation on the basis that embolism is "probable." A normal pulmonary perfusion scan in four views is strong evidence against embolism, but defects are not definitive proof that it is present

Continued on Page 253

Tenuate®
(diethylpropion hydrochloride NF)

Tenuate Dospan®
(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle, the patient should therefore be cautioned accordingly. **Drug Dependence:** Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychological dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression, changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. **Use in Pregnancy:** Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. **Use in Children:** Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: **Cardiovascular:** Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. **Central Nervous System:** Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache, rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. **Gastrointestinal:** Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. **Allergic:** Urticaria, rash, ecchymosis, erythema. **Endocrine:** Impotence, changes in libido, gynecostasia, menstrual upset. **Hematopoietic System:** Bone marrow depression, agranulocytosis, leukopenia. **Miscellaneous:** A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg tablet daily, swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSEAGE: Manifestations of acute overdose include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phenitoin (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdoseage.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.
Cayey, Puerto Rico 00633

Direct Medical Inquiries to

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TABLE 6

**CLINICAL AND LABORATORY FINDINGS ASSOCIATED WITH
HYPOXEMIA AND HYPERCAPNIA**

Hypoxemia

1. Increased sympathetic discharge—increased pulse, cardiac output, and blood pressure.
2. Direct depressant effects—vasodilatation, decreased cardiac output.
3. Central nervous system effects—confusion, loss of judgement, paranoia, restlessness.
4. Lactic acidosis.
5. Pulmonary hypertension.
6. Tissue hypoxia, death.

Hypercapnia

1. Increased sympathetic discharge—increased pulse, cardiac output, and blood pressure.
 2. Vasodilatation with headache, flushing, diaphoresis, papilledema.
 3. Pulmonary hypertension.
 4. Central nervous system depression—apathy, drowsiness, coma.
 5. Muscle twitching.
 6. Acidosis.
-

because heart failure or disease in the lung parenchyma or airways may be responsible. Even ventilation scans used in conjunction with perfusion scans are not totally satisfactory, because pulmonary embolus may lead to constricted airways as a result of the impaired perfusion. Selective angiography gives the sharpest definition of pulmonary vasculature and is most likely to provide the diagnosis. Despite having angiography as the “gold standard” for diagnosis of pulmonary embolus, we are often faced with situations where this procedure is not practical to perform or where the diagnosis seems sufficiently “clear-cut” without it. Here we must weigh the risks of anticoagulation against its potential benefits in coming to a conclusion about therapy.

Vasculitis is another form of pulmonary vascular disease. It may first appear as a relatively localized abnormality on the chest x-ray, or it may be diffuse and recurrent. The vasculitis of Wegener's granulomatosis produces recurrent fevers, and the x-rays show infiltrates at first and eventually cavitation. Because these conditions are likely to respond well to immunosuppressive therapy with cyclophosphamide or steroids, the diagnosis is important.

Pneumothorax and Pneumomediastinum

Spontaneous pneumothorax may present as mild to severe dyspnea; at times it is associated with chest pain. The patient is usually young and free of antecedent illness. History may suggest the diagnosis and physical examination support it, but a chest x-ray is needed, as a rule, to establish the presence of pneumothorax. A bleb on the surface of the lung, presumably a congenital weakness, is most commonly the cause, and the patient usually can be spared further work-up if the chest x-ray is normal. When an underlying disease such as histiocytosis X

TABLE 7

OCCUPATIONAL AND ENVIRONMENTAL LUNG DISEASES

1. Pulmonary fibrosis
 - A. Silicosis
 - B. Asbestosis
 - C. Coal worker's pneumoconiosis
 - D. Talc exposure
 2. Pulmonary infiltrative disease
 - A. Hypersensitivity pneumonias
 - B. Beryllium exposure
 3. Airways obstructive disease
 - A. Occupational asthma and bronchitis
 - B. Dust exposures such as cotton dust and flour
 4. Toxic injuries
 - A. Irritant gases (NH₃, HCl, Cl₂, SO₂, NO₂)
 - B. Thermal burns and smoke inhalation
-

TABLE 8

DRUG-RELATED PULMONARY DISEASE

1. Chemotherapeutic agents (bleomycin)
2. Nitrofurantoin (acute or chronic)
3. Narcotics (heroin, methadone)
4. Drugs causing SLE-like syndrome (procaine amide, apresoline)
5. Multiple drugs causing pulmonary infiltrate with eosinophilia
6. Mineral oil aspiration
7. Pituitary snuff reaction
8. Oxygen toxicity

Mediastinal and Hilar Changes

1. Diphenylhydantoin (hilar adenopathy)
2. Corticosteroids (lipomatosis)

Pleural Effusion

1. Acute nitrofurantoin reaction
2. Drugs inducing SLE-like syndrome

Bronchospasm

1. B-sympathetic blocking agents (propanolol)
2. Prostaglandins (of the F series)
3. Aerosols (isoproterenol, disodium chromoglycate)

Respiratory Muscle Paralysis

Antibiotics (including gentamycin, neomycin, streptomycin, polymyxin B)

(eosinophilic granuloma) or tumor is at fault, chest films usually show the abnormality. Air in the mediastinum may come from a ruptured esophagus; in this case a pleural effusion is often found. Small pneumothoraces may simply be observed, but when the volume exceeds 20 to 30 percent of the lung volume, a chest tube is required.

Environmental, Occupational, and Medical Agents

A host of substances, many of them encountered in the workplace, cause pulmonary disease (Table 7). It is essential to consider occupational or other environmental exposure when a patient develops fibrosis, hypersensitivity pneumonia, or a granulomatous process. Some of these conditions also have late sequelae—for example, the lung cancers or mesotheliomas associated with asbestosis. The list of agents known to produce pneumoconioses is continually lengthening.

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From the Secretary's Notebook

Summary of 1980 Annual Meeting of the M.M.A. House of Delegates June 12 and 13, 1980 at Dixville Notch, New Hampshire

The 127th Annual Session of the M.M.A. House of Delegates was held at The Balsams in Dixville Notch, New Hampshire with a registered attendance of 66 delegates and alternates and 21 guests. The first session was convened on Thursday, June 12 at 2:00 P.M., and the second session on Friday, June 13 at 2:00 P.M. Brinton T. Darlington, M.D., President of the M.M.A. called to order the meetings of the House, which were presided over by George W. Bostwick, M.D., Speaker of the House.

Election of Speaker and Vice-Speaker of the House of Delegates for 1980-1981—Francis I. Kittredge, M.D. was elected Speaker, and Thomas Shields, M.D. was elected Vice-Speaker.

Budget for 1981—Reference Committee recommendation that the 1981 budget be *deferred*, and that this budget be *referred* to the Executive Committee and that they be charged with developing a budget that addresses the concerns of the membership (and what direction the M.M.A. is going to be going in next year); further, that the recommendations of the Executive Committee be brought to the Fall Meeting of the House of Delegates, with a recommendation for appropriate dues structure at that time, was unanimously *approved*.

Committee on Nominations—A slate was prepared in April at the Interim Meeting of the House of Delegates and presented for vote. Nominated from the floor were Drs. Edward David (Penobscot County) and Owen Dow (York County). The following officers were elected:

President-elect

George W. Bostwick, M.D., Newcastle

Executive Committee

Gilbert R. Grimes, M.D., Lewiston
(Androscoggin County)

Albert J. Lantinen, M.D., Glen Cove (Knox County)

David P. Frasz, M.D., Dover-Foxcroft
(Piscataquis County)

Quinby D. Gurnee, M.D., Winter Harbor
(Hancock County)

Richard C. Leck, M.D., Bath
(Lincoln-Sagadahoc County)

David L. Phillips, M.D., Rumford (Oxford County)
Edward David, M.D., Bangor (Penobscot County)

Richard C. Taylor, M.D., Skowhegan
(Somerset County)

Robert B. Keller, M.D., Belfast (Waldo County)

Owen Dow, M.D., Sanford (York County)

The **Standing Committees**, constituted per recommendation of the Committee on Nominations, were *approved* with the following additions: Peter Jeffries, M.D., Committee on Allied Health Professions, Jeanne Arnold, M.D., Committee on Continuing Education, Frederick C. Holler, M.D., Chairman of the Committee on Health Care, Kenneth Hamilton, M.D., Committee on Health Care, Craig Childs, M.D., Member and Chairman of the Committee on Peer Review.

Printed Reports not requiring action and accepted for information were as follows: Committees: Amy W. Pinkham Fund, AMA-ERF, Emergency Medical Services, Health Care Finance, Peer Review, Legislation, School Health, Physicians Concerned (with commendation); Reports of Secretary-Treasurer, Executive Director, Editor, AMA Delegate, Executive Committee Chairman, Executive Committee members, Delegate to Rhode Island Medical Society, and Delegate to United States Pharmacopeial Convention.

RESOLUTIONS

Osteopathic Membership in the County Medical Society—This resolution, presented by the Piscataquis County Medical Society and amended by the Reference Committee was *approved* as follows:

WHEREAS: Mutual cooperation between the M.M.A. and the M.O.A. has become more and more a fact of life; and

WHEREAS: This cooperation is seen as an advantage to the welfare of the citizens of Maine; and

WHEREAS: The Maine Osteopathic Association now recognizes dual membership in Medical Societies;

THEREFORE BE IT RESOLVED: That if an Osteopathic Physician is a member in good standing in the M.O.A. and at the discretion of each county medical society, he may be elected to membership in the County Medical Society of the M.M.A. in the county in which he lives; with all the rights and privileges and responsibilities therein; providing he pays the appropriate dues to that County Medical Society.

Medical Liability Insurance—Submitted by the Maine Society of Internal Medicine, this resolution was *approved*:

WHEREAS: The risk of medical malpractice action to any particular category of physicians is variable and dynamic, requiring frequent study and updating of loss experience data; and

WHEREAS: There is general agreement that medical liability insurance premiums should reflect the actual cost and risk of providing insurance to any particular category or group;

THEREFORE BE IT RESOLVED: That the Maine Medical Association (*state medical association*) supports the concept that premium schedules for medical liability insurance should be based on the actual cost and risk of providing that insurance to each individual group or category.

Committee on Investments and the Budget—Presented by the Executive Committee, this resolution was *approved*:

WHEREAS: Sound financial planning requires knowledge and time, two attributes not always available to members of the Executive Committee; and

WHEREAS: The Executive Committee desires to avail itself of the help of others in exercising its duty to manage Association finances; now

THEREFORE BE IT RESOLVED: That Section 10 of Chapter V of the Bylaws shall be and is hereby amended to read, "*Section 10.* The Executive Committee shall appoint a Committee on Investments and the Budget, consisting of three (3) members, whose duty it shall be, under the direction of the Executive Committee, to invest, reinvest, and change investments, of such monies, securities, and funds of the Association as are available to it or held in trust, to review the lists of such assets, and to prepare proposed budgets and reports of the financial condition of the Association for the Executive Committee as requested by that body. The terms of the members of the Committee on Investments and the Budget shall be for three years, with terms staggered so that one member shall be appointed each year. Members may be asked to succeed themselves."

Deadline date for payment of dues—Presented by the Executive Committee, this resolution was *approved*:

WHEREAS: Fiscal responsibility requires the Maine Medical Association to plan to expend no more than its annual income; and

WHEREAS: Timely collection of dues monies allows timely budgetary planning; now

THEREFORE BE IT RESOLVED: That Section 1A of Chapter VIII of the Bylaws shall be and is hereby amended by changing from June 1 to April 1 the day on which a delinquent member shall stand suspended.

Executive Committee Meetings—Presented by the Executive Committee, this resolution was *approved*:

WHEREAS: The onus of daily meetings before and during each Annual Session discommodes an increasing number of people when there are not necessarily many important matters to come before the Executive Committee at that particular time; now

THEREFORE BE IT RESOLVED: That Section 1 of Chapter V of the Bylaws shall be and is hereby amended by deleting the sentence "The Executive Committee shall meet on the day preceding the Annual Session, and daily during the Session," and substituting therefore the following sentence: "The Executive Committee shall meet the first day of the Annual Session and thereafter as it deems necessary."

Continuing Education—Presented by the Executive Committee, this resolution was *approved*:

WHEREAS: Continuing Medical Education has now become a requirement for licensure to practice medicine in the State of Maine, rendering inappropriate the monitoring by the Maine Medical Association of CME participation by members; now

THEREFORE BE IT RESOLVED: That the following sections of the Bylaws shall be and are hereby deleted: Section 11 of Chapter I, in its entirety; The penultimate sentence of Section 4 of Chapter V; The penultimate paragraph of Subsection D of Section 4 of Chapter VII.

Standing Committees—Presented by the Executive Committee, this resolution was *approved*:

WHEREAS: Reassessment of the need for and functions of the various standing committees is a responsibility of the Executive Committee, who have noted changes in the concerns and challenges of M.M.A. since the current Bylaws were formulated, with the result that the Executive Committee recommends; that

THEREFORE BE IT RESOLVED: That Chapter VII of the Bylaws shall be and is hereby amended by deletion, in Section 2, of Committee on Care of the Disadvantaged, Committee on Emergency Medical Service, and Committee on Hospital Liaison from the COUNCIL ON MEDICAL SERVICES, and Committee on Professional Liability from COUNCIL ON MEDICINE AND LAW; and Further,

BE IT RESOLVED: That Subsection C of Section 3 of Chapter VII shall be and is hereby deleted in its entirety; and further,

BE IT RESOLVED: That Subsection D of Section 3 of Chapter VII shall be and is hereby deleted in its entirety; and further,

BE IT RESOLVED: That Subsection F of Section 3 of Chapter VII shall be and is hereby deleted in its entirety.

BE IT RESOLVED: That Subsection C of Section 5 of Chapter VII shall be and is hereby deleted in its entirety.

Committee on Health Care Financing—Presented by the Executive Committee, this resolution was *approved*:

BE IT RESOLVED: That the Committee on Health Care Financing be renamed Committee on Health Care by eliminating the word Financing wherever it appears in the name of this committee in Paragraph 2 of Article VI of the Constitution and in Sections 2 and 3 of Chapter VII of the Bylaws; and further

BE IT RESOLVED: That Subsection A of Section 3 of Chapter VII of the Bylaws shall be and is hereby amended by substitution, for the last sentence in the first paragraph, of the sentence "It shall study the economic conditions of health, of medical care, of hospital services, of public health services, and all other germane subjects in all areas of the State, and make recommendations for their improvement."

Maine Medical Education Foundation—Presented by the Executive Committee, this resolution was taken up in two parts. The first, asking that the word "allopathic" be inserted before the word "Medicine" was *defeated*. The second part was *approved* with an amendment, as follows:

BE IT RESOLVED: That the following new second paragraph be inserted between the current first and second paragraphs of Chapter VII-A of the Bylaws: "The Maine Medical Association, as Trustee for the Maine Medical Education Foundation, shall have the Authority to buy, sell, lease, and otherwise act with respect to personal and real property, the income therefrom to be used solely for the purposes noted in paragraph one. Transactions involving real property shall be undertaken only with the approval of the Executive Committee. Once such transactions are approved, the President, the Executive Director, or the Secretary-Treasurer may execute any necessary documents authorized by the Committee."

Allied Health Professions Committee—Presented by the Executive Committee, this resolution was *approved*:

WHEREAS: The Committee on Allied Health Professions wishes to have its charge more closely parallel the functions it has traditionally served;

NOW THEREFORE BE IT RESOLVED: That the entire first paragraph of subsection B of Section 4 of Chapter VII shall be and is hereby amended by substitution of the following:

This committee shall consist of at least (5) members. The committee shall establish a liaison with the professional organizations of counterpart clinicians at the state level to assure that avenues of discussion about mutual concerns are maintained.

The interchange of ideas among allied health groups and questions about the evaluation or quality of training programs for allied health professionals shall be the purview of this committee.

Government Health Activities—Presented by the Executive Committee, this resolution was *approved*:

WHEREAS: The spheres of interest and function of the Committee on Government Health Activities and on Legislation overlap;

Now, THEREFORE BE IT RESOLVED: That Section 2 of Chapter VII of the Bylaws shall be and is hereby amended by deletion of mention of Committee on Government Health Activities, and that Subsection B of Section 3 be deleted and subsequent subsections relettered appropriately:

and, FURTHER BE IT RESOLVED: That the first paragraph of Subsection A of Section 5 of Chapter VII of the Bylaws shall be and is hereby amended by substitution for the second sentence of the following: "This committee shall be charged with the direction and coordination of all Association activities related to State and Federal health programs and with study of all matters of professional interest to this Association which are considered by the State Legislature."

M.M.A. Health Care Coverage—The report of the Ad Hoc Committee on Health Care was *approved*, as were the following resolutions:

THAT members of the Maine Medical Association would be willing to get a lesser cost, greater benefit policy with a front end deductible.

THAT the members of the Maine Medical Association would be willing to consider a policy conditional upon the purchase of term life insurance.

Nuclear Power—The following policy statement, presented from the floor, was *approved*:

The Maine Medical Association is unable to take a benefit/risk position on the relative risks stemming from nuclear and other forms of energy. Since we operate on the basis of science and medicine this is obviously beyond our expertise. And if we cannot make this kind of judgment, we cannot take a position either for or against nuclear power.

The M.M.A. is, of course, primarily interested in the control of cancer and the safety of our patients. But the control of cancer that might be caused by the various techniques used to manufacture electrical power is far beyond M.M.A. capacities or expertise.

It is clear that the public perception of ionizing radiation accents danger or risk over benefit.

It is equally clear that while the potential of danger is great, mainly from weapons, the actual harm of radiation is small in relation to its benefits in medicine and the economy. Radiation has been well studied and, so far in medicine and industry,

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CONTINUING MEDICAL EDUCATION IN MAINE

Conferences and Workshops

Title: Family Medicine Update
Date: September 7-10, 1980
Location: Spruce Point Inn, Boothbay Harbor
Sponsors: AAFP and Medical Care Development
Credit: AMA and LCCME Category I—15 hours and AAFP (prescribed)—14 hours
Reg. Fee: \$150; \$120 for State of Maine AAFP members
For further information contact Gerald Goold, Medical Care Development; 622-7566.

Title: Practical-Clinical Cardiology Conference
Date: September 26-28, 1980
Location: Auditorium, Jackson Laboratories, Bar Harbor
Sponsor: American Heart Association, Maine Affiliate
Credit: AMA and LCCME Category I—12½ hours and AAFP (elective)—5 hours
Reg. Fee: To be determined

Title: Third Annual Infectious Diseases Symposium
Date: September 27, 1980
Location: Schaeffer Theater, Bates College
Sponsors: St. Mary's General Hospital, Central Maine Medical Center, and Bates College
Credit: AMA and LCCME Category I—6 hours and AAFP (elective) 6 hours
Reg. Fee: \$10.00

Title: Maine Prevention Conference
Date: October 21-22, 1980
Location: Holiday Inn, Downtown, Portland
Sponsor: National Council on Alcoholism in Maine, Office of Alcoholism & Drug Abuse Prevention
Credit: AMA and LCCME Category I being applied for.
Reg. Fee: \$40

Title: Tri-State Surgical Association Annual Meeting
Date: November 6-9, 1980
Location: Castle Harbor Hotel, Bermuda
Sponsor: Maine Chapter, American College of Surgeons
Credit: AMA and LCCME Category I—18 hours
Reg. Fee: To be determined
For further information contact John Towne, M.D.; 872-7713.

Programs Sponsored By Mid-Maine Medical Center/Colby College

Title: Nuclear Medicine
Date: August 17-21, 1980
Credit: AMA and LCCME Category I—28 hours
Title: Medical and Surgical Emergencies
Date: August 19-22, 1980
Credit: AMA and LCCME Category I; AAFP (prescribed)—25 hours

Title: Forensic Science
Date: August 24-27, 1980

Sponsors: In cooperation with the National Association of Medical Examiners

Credit: AMA and LCCME Category I; AAFP—24 hours

Title: Pulmonary Disease

Date: August 24-28, 1980

Credit: AMA and LCCME Category I—21 hours

All of the Colby activities will be based at the Colby College campus in Waterville. Registration fee is to be determined. For further information contact Robert Kany, Ph.D., Colby College; 873-1131 Ext. 267/251.

Hospital Activities

Central Maine Medical Center Lewiston, Maine

Every Thurs.	Tumor Board	12-1 p.m.
Every Friday	Medical Grand Rounds	9-10 a.m.
4th Friday (Odd Months)	Joint Surgical Grand Rounds	7:45-8:45 a.m.
2nd Fridays	Visiting Professorship, Boston University	1-3 p.m.

All activities have been certified AMA and LCCME Category I. For further information contact Palmer Jones; 795-2434.

Eastern Maine Medical Center Bangor, Maine

Every Mon.	EEG Conference	12-1 p.m.
Every Mon.	Surgical Service—Chief's Rounds	5-6 p.m.
4th Mon.	ENT Section Meeting	12-1 p.m.
4th Mon.	Neurosurgery Section Meetings	4-5 p.m.
3rd Tues.	Dermatology-Pathology Conference	5-6 p.m.
3rd Tues.	Dermatology Section Meeting	6-7 p.m.
4th Tues.	Pulmonary Medicine Section Meeting	8-9 a.m.
1st Wed.	Hematology/Oncology Meeting	8-9 a.m.
Every Wed.	Tumor Clinic Conference	2-5 p.m.
Every Wed.	Radiology Conference	5-6 p.m.
	(1) Ultrasound/Nuclear Medicine	
	(2) Radiology Film Review	
	(3) Neuroradiology	
	(4) Teaching File Conference	
	(5) G.I. Radiology	
1st Thurs.	Ophthalmology Section Meeting	7:30-8:30 a.m.
	OB-GYN Conference	8-9 a.m.
	(1) Pathology	
	(2) GYN Analysis	
	(3) OB-Pediatric Combined	
	(4) In-Service and Education	
Every Thurs.	Pediatric Grand Rounds	9-10 a.m.
Every Thurs.	Medical Service Conference	10-11 a.m.
Every Thurs.	Cardiology Conference	11 a.m.-1 p.m.

2nd Thurs.	Orthopedic Grand Rounds	7:45-8:45 a.m.
4th Thurs.	Orthopedic Service Meeting	7:30-9 a.m.
4th Thurs.	Surgical Service Death Review	7:45-8:45 a.m.
Every Thurs.	Psychiatric Service Grand Rounds	10-11 a.m.
4th Thurs.	Urology Section Conference	7:30-8:30 a.m.
Every Fri.	Neurology Grand Rounds	8-9 a.m.

Visiting Professor Program:

2nd Thurs.	Medical Service Visiting Professor	10 a.m.-5 p.m.
2nd Thurs.	Anesthesia Service Visiting Professor	7-8 a.m.
3rd Thurs.	OB/GYN Service Visiting Professor	10 a.m.-4 p.m.
Saturdays	Surgery Service Visiting Professor	8 a.m.-Noon
4th Thurs.	Pediatric Service Visiting Professor	10 a.m.-5 p.m.

as scheduled Orthopedic Service Visiting Professor

as scheduled Family Practice Visiting Professor

as scheduled Psychiatric Service Visiting Professor

All activities have been certified AMA and LCCME Category I. For further information contact James F. Lawsing, III, M.D., Coordinator, Medical Education Committee; 947-3711 Ext. 2303.

A. R. Gould Memorial Hospital Presque Isle, Maine

Every Thurs. Tumor Conference
8 a.m.

2nd Thurs. Perinatal Conference
11:30 a.m.

1st and 3rd Fri. Tumor Conference

The tumor conferences will be held in the Rotary Regional Educational Center and the perinatal conference will be held in Conference Room A. These conferences have been certified AMA and LCCME Category I. For further information contact Marilyn Dean; 769-2511.

Kennebec Valley Medical Center Augusta, Maine

Sept. 23, 1980 **Radionuclide Studies in Cardiology**
7:30-8:30 a.m. Russell Briggs, M.D., Maine Medical Center
ITS Presentation

This program has been certified AMA and LCCME Category I and AAFP (prescribed). For further information contact Mrs. Nancy Favorite; 623-4711 Ext. 333.

Maine Medical Center Portland, Maine

Special Conferences

Title: **Michael G. Waddle and David Fournier Memorial Lectures on Hypothermia and Cold Water Immersion**

Date: September 11, 1980

Location: New Diagnostic Facility Classrooms #3 & 4

Sponsors: Emergency Medical Services; American Trauma Society, Maine Division; and Maine Medical Center

Credit: AMA and LCCME Category I—3 hours

Reg. Fee: None

Title: **Albert Aranson Teaching Day**

Date: October 24, 1980

Location: New Diagnostic Facility Classrooms #3 & 4

Sponsor: Maine Medical Center

Credit: AMA and LCCME Category I—3 hours

Reg. Fee: None

Hospital Activities

Every Mon. Student Technologist Conference 8 a.m.

Every Mon. Hematology-Pathology Conference 11 a.m.
Every Mon. Pulmonary Conference 12 Noon
Every Mon. Pediatric Residents' Conference 1 p.m.
Every Mon. Anesthesia Formal Resident Lecture 3:30 p.m.
Every Mon. Surgical Pathology Review 4 p.m.
Every Mon. Radiology Journal Club 5 p.m.
1st & 3rd Mon. Clinical Nephrology Conference 11 a.m.

1st & 3rd Mon. Hematology-Pathology Conference 12 Noon

3rd Mon. Eye Conference 11:45 a.m.

Every Tues. Radiology Residents' Seminar 7 a.m.

Every Tues. Family Practice Grand Rounds 9 a.m.

Every Tues. Electrocardiographic Interpretation 1 p.m.

Every Tues. Psychiatric Grand Rounds 1:30 p.m.

Every Tues. Anesthesia Formal Resident Lecture 3:30 p.m.

Every Tues. Surgical Seminar 4 p.m.

Every Tues. Pathology Slide Seminar 4 p.m.

1st & 3rd Tues. Radiology-Pathology Conference 12 Noon

1st & 4th Tues. Neurology Conference 12 Noon

2nd Tues. Infectious Disease Conference 12 Noon

3rd Tues. Hematology Conference 12 Noon

5th Tues. Oncology Conference 12 Noon

Every Wed. Radiation Therapy Conference 7 a.m.

Every Wed. Urology Conference 7 a.m.

Every Wed. Student Technologist Conference 8 a.m.

Every Wed. Continuing Education Seminar 8 a.m.

Every Wed. Medical Conference 9 a.m.

Every Wed. Psychiatric Journal Club 12 Noon

Every Wed. Cardiology Seminar 12 Noon

Every Wed. Surgical Grand Rounds 5 p.m.

2nd Wed. Guest Internist—Medical Conference 9 a.m.

4th Wed. Medical Mortality Conference 9 a.m.

Alt. Wed. Neurology-Psychiatry Seminar 11 a.m.

Alt. Wed. Anesthesiology Journal Club 3 p.m.

Every Thurs. Thoracic Surgery Conference 7 a.m.

Every Thurs. OB/GYN Conference 7 a.m.

Every Thurs. Anesthesiology Clinical Conference 7 a.m.

Every Thurs. Diagnostic Radiology Teaching Conference 7 a.m.

Every Thurs. Surgical Conference 8 a.m.

Every Thurs. Pediatric Conference 9 a.m.

Every Thurs. Tumor Consultation Board 11 a.m.

Every Thurs. Medical Residents' Conference 12 Noon

Every Thurs. Surgical Seminar 4 p.m.

Every Thurs. Endocrinology Conference 5 p.m.

Every Thurs. Dental Specialty Lecture 6 p.m.

1st Thurs. Anesthesia Mortality Conference 7 a.m.

1st Thurs. Guest Pediatrician 9 a.m.

1st Thurs. Gastroenterology Conference 12 Noon

1st & 3rd Thurs. Cardiac-Surgical Conference 12:30 p.m.

1st, 3rd, & 5th Thurs. Pulmonary-Physiology Conference 12:30 p.m.

2nd Thurs. Cardiology Teaching Conference 12:30 p.m.

2nd Thurs. Clinical Anesthesiology Lecture Series 3:30 p.m.

2nd Thurs. Eye Staff Scientific Session 5:30 p.m.

2nd Thurs. Maine Medical Center Medical Staff Meeting and Scientific Session 6 p.m.

2nd & 4th Thurs. Pulmonary-Pathology Conference 12 Noon

2nd & 4th Thurs. Endocrinology Conference 12 Noon

3rd Thurs.	Combined Guest Physician or Guest Surgeon Program	8 a.m.
3rd Thurs.	Clinical Anesthesiology Lecture Series	3:30 p.m.
4th Thurs.	Surgical Mortality Conference	8 a.m.
4th Thurs.	Anesthesia Mortality Conference	3:30 p.m.
Last Thurs.	Pediatric Mortality Conference	9 a.m.
Every Fri.	Thoracic-Surgical Conference	7 a.m.
Every Fri.	Nuclear Medicine Conference	7 a.m.
Every Fri.	Student Technologist Conference	8 a.m.
Every Fri.	Neurological-Neurosurgical Conference	8:30 a.m.
Every Fri.	Gastroenterology Conference	9 a.m.
Every Fri.	Medical Rehabilitation Staff Conf.	9 a.m.
Every Fri.	Orthopedic Conference	9 a.m.
1st Fri.	Dermatology Conference	12 Noon
2nd Fri.	Nephrology Conference	12 Noon
3rd Fri.	Rheumatology Conference	12 Noon
4th Fri.	Oncology Conference	12 Noon
Alt. Fri.	Oncology-Radiation Conference	7 a.m.
Alt. Fri.	Gastroenterology Conference	10 a.m.

All programs have been certified AMA and LCCME Category I. For further information contact Costas T. Lambrew, M.D.; 871-2111.

Mid-Maine Medical Center Waterville, Maine

August 21, 1980	Newer Agents in RX of Hypertension Paul Parker, M.D., Maine Medical Center
August 28, 1980	Case Presentation Family Practice Residents
Sept. 4, 1980	Clinical Pathological Conference (Medical Staff Only)

Ongoing Activities

Every Mon.	Ophthalmology	8-10:30 p.m.
Every Tues.	Tumor Board	12 Noon-1 p.m.
Every Tues.	Regional Infectious Disease ITS presentation	12 Noon-1 p.m.
3rd, 4th, & 5th Tues.	Obstetrics with Augusta General Hospital	12 Noon-1 p.m.
Every Wed.	Regional Pulmonary Disease ITS presentation	12 Noon-1 p.m.

Every Thurs.	Medical-Surgical Conference	12 Noon-1 p.m.
Thurs.-Weekly	Regional Pathology	1-2 p.m.
Thurs.-Monthly	Department of Medicine	6-7:30 p.m.
Every Fri.	Anesthesiology	6:30-7:30 a.m.
Every Fri.	Orthopedics	7-8 a.m.
Every Fri.	Pediatrics	12 Noon-1 p.m.
2nd Fri.	General Surgery	7-8 a.m.
4th Fri.	Surgical Audit	12 Noon-1 p.m.

All activities have been certified AMA and LCCME Category I. The Medical-Surgical Conference on Thursday has also been certified AAFP (elective). All are ITS presentations excluding CPC. For further information contact David R. Ginder, M.D.; 873-0621.

St. Mary's General Hospital Lewiston, Maine

Every Tuesday	Medical Grand Rounds	8-9 a.m.
1st and 3rd Fridays	Tumor Conference	12-1 p.m.
Last Friday of month	Surgical Grand Rounds	12-1 p.m.

The Surgical Grand Rounds will be alternating monthly between St. Mary's General Hospital and Central Maine Medical Center. These activities have been certified AMA and LCCME Category I. For further information contact Michael C. Bach, M.D.; 783-2227.

V. A. Hospital Togus, Maine

Every Wednesday	Medical Staff Service Meetings	1:15-2:15 p.m.
Every other Thurs.	Oncology Clinic	2-3 p.m.
2nd Tues. of month	Psychiatric CME Meetings	

These activities have been certified AMA and LCCME Category I. For further information contact E. Osborne Coates, Jr., M.D., VAM and ROC, Togus; 623-8411.

ANNOUNCEMENT: Medical Care Development, Inc. is now receiving a listing of continuing medical education activities taking place in Vermont, New Hampshire, and Massachusetts. If you wish further information contact Gerald Goold, Medical Care Development; 622-7566.

DIAGNOSTIC IMPERATIVES IN INTERNAL MEDICINE—Continued from Page 253

Likewise, the number of drugs causing pulmonary disease is increasing (Table 8). A variety of idiosyncratic or allergic reactions is seen. Pulmonary fibrosis may result from exposure to anti-cancer agents, such as bleomycin, or the antibiotic nitrofurantoin. Pulmonary edema is a known complication from the use not only of heroin but its analog methadone. A syndrome resembling systemic lupus erythematosus is triggered by procaine amide, apresoline, and other agents. Pulmonary infiltrates and peripheral eosinophilia can be caused by many drugs, presumably acting as allergens. Inhaled mineral oil or pituitary snuff may produce a reaction, and high concentrations of inspired oxygen (greater than 40 to 60 percent) can injure the lung.

Milder reactions also occur; for example, phenytoin can cause hilar adenopathy, and use of corticosteroids may lead to the deposition of lipids in the mediastinum which appear as a mass on chest films.

Beta-sympathetic blockers may accentuate bronchospasm, and even therapeutic aerosols may backfire by increasing the irritability of airways. Several antibiotics, by interfering with nerve transmission, can produce respiratory paralysis.

It is particularly important for the physician to be conscious of the possibility that he is administering agents that are potentially injurious.

COMMENT

At present, such common terms as chronic obstructive lung disease, chronic bronchitis, asthma, pulmonary fibrosis, interstitial pneumonia, and sarcoidosis are descriptive and not etiologic. We can hope that as the etiology of these conditions is elucidated, physicians will be challenged to make ever more precise diagnoses and gratified by more effective treatments.

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Necrologies

RALPH A. GOODWIN, SR., M.D.

1884-1980

Dr. Ralph A. Goodwin, Sr., 95, of Auburn Maine, former President of the Maine Medical Association from 1949-1950, died on April 18th at his home following a long illness.

Born in Danforth, Maine on December 13, 1884, he was the son of Ella M. and Herbert Goodwin.

Dr. Goodwin was graduated from Bates College and received his medical degree from Harvard Medical School in 1913. He served an internship at the Rhode Island Hospital and took postgraduate courses at the Massachusetts General Hospital and Central Maine Medical Center in Lewiston.

He had practiced in Auburn since 1920, and was a member of the surgical staff at the Central Maine General Hospital, and a member of its active and consulting staff until 1975, when he was designated an honorary surgeon. From the early 1920's until 1947, he was physician to Bates College.

An honorary member and Past President of the Androscoggin County Medical Society and the Maine Medical Association, he received a 50-year pin in 1963, a 55-year pin in 1968, a 60-year pin in 1973 and a 65-year pin in 1978. Dr. Goodwin was President-elect of the M.M.A. from 1948-1949, Council Chairman in 1947-1948 and, prior to that, had served as Councilor for the Second District. He was also a member of the American Medical Association and a fellow of the American College of Surgeons.

Surviving is a son, Dr. Ralph A. Goodwin, Jr. of Auburn and two daughters, Mrs. Robert York of Gorham and Mrs. Marguerite Anderson of Ann Arbor, Michigan.

ORY D. CANAL, M.D.

1910-1980

Dr. Ory D. Canal, 69, of Augusta, Maine, died on July 1st at his home.

He was born in Havana, Cuba on December 22, 1910, the son of Alfred and Josephine P. Canal.

Dr. Canal attended schools in Havana, Cuba and received his medical degree from the University of Paris, France in 1940. He interned at St. Joseph's Hospital in Lorain, Ohio and served a residency at Eastern State Hospital in Washington.

He practiced in Lorain, Ohio and the State of Washington, and in 1955, located in Augusta where he was affiliated with the Augusta State Hospital. From 1965 until the time of his death, he was affiliated with the Veterans Administration Center in Togus.

Dr. Canal was a member of the Kennebec County Medical Association, the Maine Medical Association, the American Psychiatric Association and the Maine Psychiatric Association.

He is survived by his wife, the former Esther M. Ragusa of Augusta; two sons, Patrick Canal of Miami, Florida and Ory J. Canal of Augusta; two sisters, Mrs. Rachel Symington and Miss Delia Canal, both of Miami, Florida; and several nieces and nephews.

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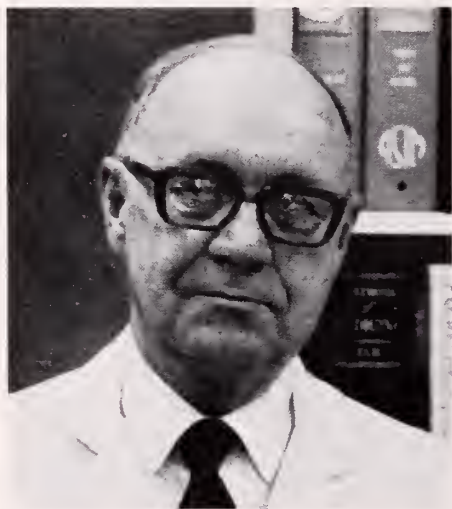
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*PATIENT CARE Magazine—Outlook 1977 "Face-Off: Cost Containment vs. Chaos," January 1, 1977

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Schroeder SA, et al. "Use of laboratory tests and pharmaceuticals: variation among physicians and effect of cost audit on subsequent use," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 225 (Aug. 20, 1973), 969-73.



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The Journal of the Maine Medical Association

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Augusta, Maine, September 1980

Number 9

Cardiac Transplantation

Case Report and Current Status

PAUL R. MINTON, M.D.*

On February 3, 1977, an 18-year-old student from Cape Elizabeth, Maine, underwent successful cardiac transplantation at Stanford University Medical Center, Stanford, California, by Dr. Norman Shumway and his associates because of severe, disabling congestive heart failure due to cardiomyopathy. More than three years later, now over 21 years of age, he has completed his second year of college, notes no cardiac symptoms and enjoys normal exercise tolerance limited only by ankle discomfort. He is the first Maine resident to undergo cardiac transplantation.

CASE REPORT

HISTORY

S.P. was the product of a normal pregnancy and delivery; although growth and development were normal, he experienced a severe illness, consistent with infectious mononucleosis, at age three years. At no time during infancy, childhood or adolescence was there any evidence of heart disease or heart murmur and he enjoyed normal exercise tolerance until late 1975, when cough and mild dyspnea occurred. In January 1976, chest film performed for evaluation of symptoms showed marked cardiomegaly. On cardiac evaluation, he was a robust, healthy appearing young man, weighing 180 lbs, 73½" in height. Pulse 78 and regular, blood pressure 126/62 both arms. There was no cyanosis, clubbing or edema, peripheral pulses were normal in volume, bilaterally equal, there were no arterial bruit. Jugular venous pressure was not increased; the lungs were clear. The abdomen was normal without tenderness or hepatomegaly. Abnormal cardiac findings were: diffuse left ventricular lift, S3 and S4 gallops and a faint apical mid-systolic murmur.

ECG (Fig. 1A) showed premature ventricular beats, low QRS voltage, left atrial and right ventricular enlargement.

CHEST X-RAY (Fig. 2A) showed marked, diffuse cardiomegaly, small aortic arch, and no evidence of pulmonary congestion.

ECHOCARDIOGRAM (Fig. 3A) showed marked left ventricular dilatation with mild hypertrophy, decreased posterior LV wall systolic velocity and amplitude, and left atrial enlargement.

No valvular abnormality was noted. Echocardiogram was consistent with congestive cardiomyopathy.

CARDIAC CATHETERIZATION (Table 1) performed at Maine Medical Center demonstrated evidence of severe left ventricular dysfunction manifested by marked LV dilatation, marked impairment in contractility, abnormal intracardiac pressures. The coronary arteries were normal. Resting cardiac index was reduced to 2.1 L/MIN/M² and increased to 4.3 L/MIN/M² with exercise.

Aspirin was prescribed as an antiplatelet agent and activity restriction was advised. He remained free of cardiac symptoms until August 24, 1976, when hospitalization was required for four days because of migraine headaches, nausea and vomiting. There was no evidence of pulmonary congestion. Liver tenderness and abnormal function tests suggested visceral congestion. Symptoms were relieved following bed rest and digoxin. Over the next month, gradual recurrence of abdominal bloating and epigastric tenderness occurred. For the first time, dyspnea and hemoptysis were noted requiring hospitalization on September 29, 1976. Although jugular venous pressure did not appear increased and the lungs were clear, there was considerable epigastric tenderness and hepatomegaly. Mild pulmonary congestion was noted on chest film, perfusion lung scan was negative for pulmonary emboli. Digoxin was continued and with administration of diuretics he improved considerably, lost 14 pounds, and was discharged on 10/8/76. Increasing fatigue, exertional dyspnea, orthopnea, hemoptysis, and symptomatic visceral congestion recurred despite an intensive diuretic regimen. Cardiac cachexia became evident with muscle wasting and weight loss despite fluid retention. Medical treatment offered no hope for improvement and little hope for long-term survival. Cardiac transplantation seemed the only alternative. The institution in the United States performing the largest number of cardiac transplantations was Stanford University Medical Center, Stanford, California. The Stanford criteria for selection of patients for cardiac transplantation (Table 2) and the contraindications (Table 3) were reviewed. Comprehensive psychiatric evaluation was performed on 11/8/76 and there were no psychiatric or psychosocial contraindications. The information was sent to Stanford for review and S.P. was accepted for evaluation.

On 11/29/76, S.P. left Maine for Stanford University Medical Center where he was hospitalized through 12/4/76 for cardiac evaluation. Physical findings were not changed, repeat cardiac catheterization confirmed severe impairment in LV contractility and a decrease in cardiac index to 1.8 L/MIN/M². Percutaneous right internal jugular vein RV endomyocardial biopsy, a routine procedure for cardiac transplantation candidates, was performed. The result was post-viral cardiomyopathy. On 12/3/76, S.P. was accepted for transplantation. Ten days later, he was again

*From the Division of Cardiology, Department of Medicine, Maine Medical Center, Portland, Maine 04102.

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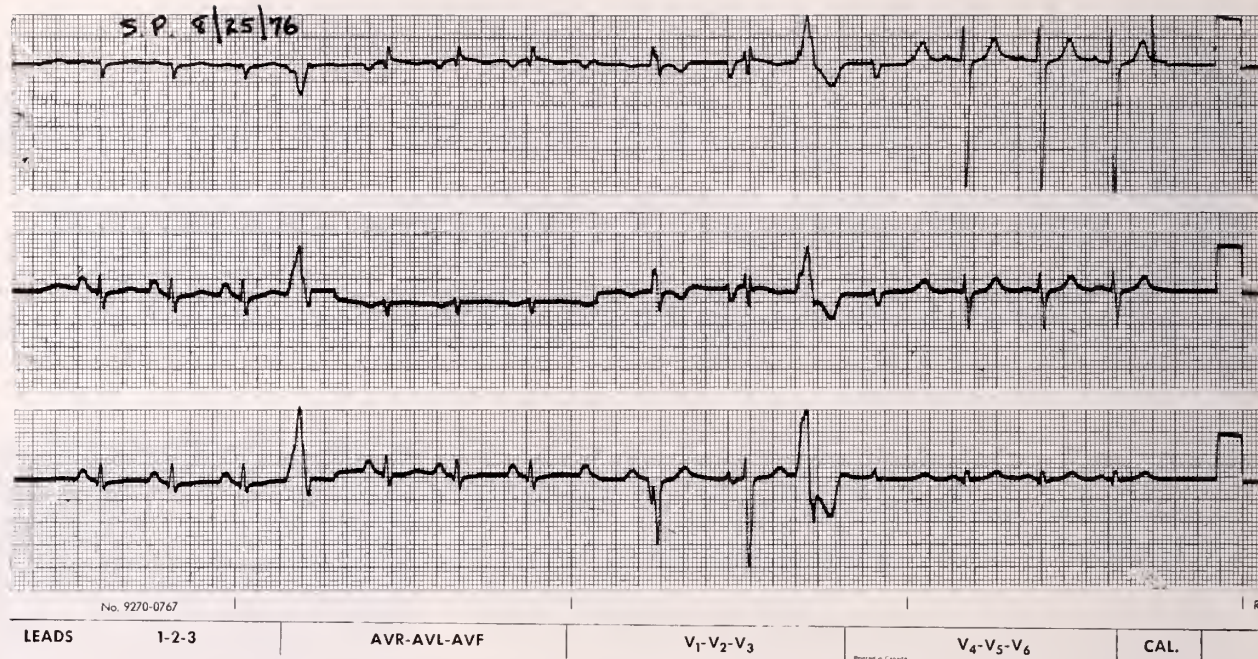


Fig. 1A. Preoperative Electrocardiogram.



Fig. 2A. Preoperative Chest Film.

hospitalized because of pulmonary embolism and infarction; his name was removed from the "list" for transplantation. Improvement followed treatment with heparin and on 1/13/77 he was again accepted for transplantation. The operation was performed on 2/3/77. Examination of his heart at operation was consistent with cardiomyopathy showing diffuse, marked chamber dilatation with multiple intraventricular thrombi. The ventricles were diffusely fibrotic and paper thin.

The initial postoperative course was satisfactory. Acute rejection occurred on 2/10/77 but responded to antihuman thymocyte globulin and an increase in the usual doses of immunosuppressive agents. Post transplantation course was then one of prompt

restoration of normal vigor and effort tolerance, in contrast to the weeks before transplantation when he was bedridden, experiencing dyspnea on slightest effort and almost continuous cough and hemoptysis. A permanent VVI RV endocardial pacemaker was implanted on 3/29/77 because of symptomatic sinus bradycardia and he was discharged from Stanford University Medical Center on 4/3/77, exactly two months following transplantation. After two months in the Palo Alto area where he had weekly checkups, S.P. returned home to Cape Elizabeth, Maine. By 6/3/77, he enjoyed entirely normal effort tolerance, but required an intensive regimen of immunosuppressive agents, diuretics and anticoagulants (Table 4). During the summer of 1977, he enjoyed normal, vigorous physical activity and jogged, played tennis and waterskied. Regular cardiac examinations were performed including a specific technique of ECG recordings, chest films and appropriate blood tests. ECG (Fig. 1B) showed sinus rhythm, normal QRS voltage, and T wave changes which gradually cleared over several months. Although two atrial rhythms (from donor and recipient) are often visualized in the ECG of cardiac transplant patients, these were not clearly noted in S.P. Chest film (Fig. 2B) showed normal heart size. Echocardiogram (Fig. 3B) demonstrated normal LV dimensions, normal LV contractility and paradoxical motion of LV septum, a nonspecific finding after most cardiac operations. On 8/4/77, coincident with reduction in prednisone to 25 mg per day, decrease in ECG voltage and development of atrial flutter indicated mild cardiac rejection. Prednisone was increased to 100 mg daily, cardiac rate was slowed with digoxin, ECG voltage returned to previous values and atrial flutter spontaneously converted to sinus rhythm on 8/11/77. On 8/23/77, he was hospitalized because of left posterior pleuritic chest pain and infiltrate in the apical segment of the left lower lobe, suspected due to infection with an opportunistic agent. Medications were as shown in Table 4 except for dose of prednisone 50 mg daily. Cardiac examination was normal; there were wheezes at the left lung base posteriorly. Chest films and tomography confirmed a nodular density in the apical segment of the left lower lobe posteriorly with no evidence of any other abnormality. Sputum smear was not diagnostic. Direct needle aspiration of the pulmonary lesion demonstrated typical *Nocardia* on smear. Cultures confirmed *Nocardia*, sulfisoxazole 12 GM daily was begun and the density on chest film gradually cleared over the next month.

S.P. returned to complete his senior year of high school in September 1977, and continued to feel well except for ankle pain and fragile skin, particularly of the lower extremities, both side effects from steroids. Between early October and late December

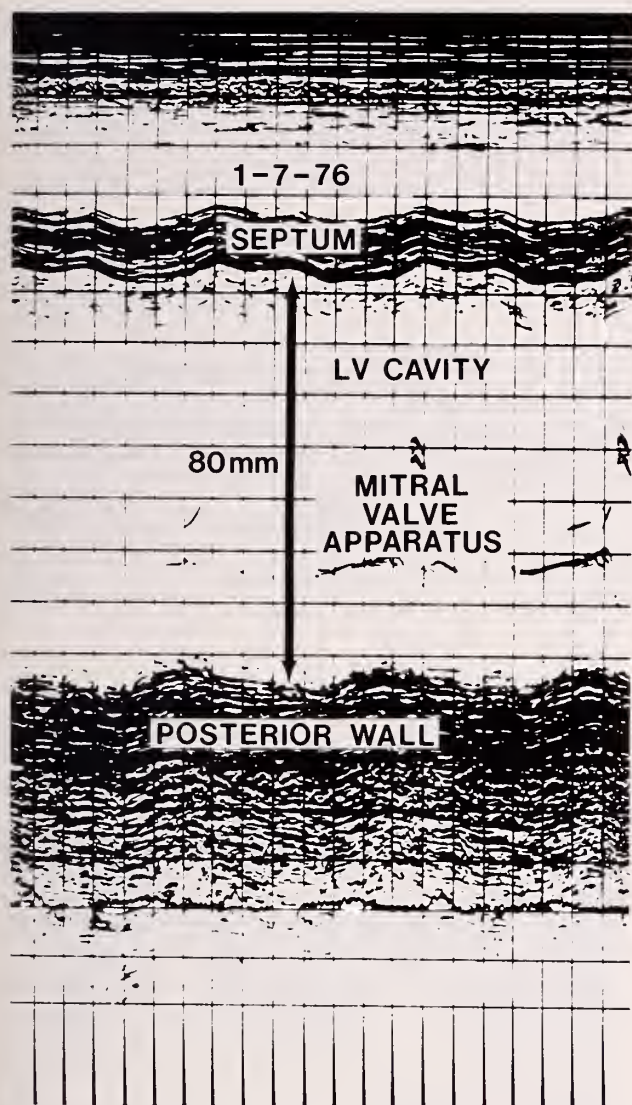


Fig. 3A. Preoperative Echocardiogram.

1977, he continued to feel well; prednisone was reduced to 25 mg per day. In late December 1977, a loud S3 gallop was noted but there was no significant decrease in ECG voltage. For definite confirmation or exclusion of rejection, S.P. was hospitalized at Stanford University Medical Center on 1/2/78 and underwent repeat right and left cardiac catheterization, coronary arteriography and right ventricular endomyocardial biopsy. Hemodynamic and arteriographic findings were all within normal limits and endomyocardial biopsy excluded rejection. Because of decrease in total WBC to 3200 cells/mm³, azathioprine was reduced to 100 mg per day. Presumably the large dose of sulfisoxazole had produced additional immunosuppressive effect. Ophthalmologic examination showed early cataracts due to steroids. On 5/2/78, because of definite decrease in ECG voltage without any clinical signs of hemodynamic impairment, early rejection was suspected, prednisone was increased from 25 mg to 100 mg daily with prompt restoration of ECG voltage to its usual level. This second rejection after returning to Maine may have been due to reduction in azathioprine dose following endomyocardial biopsy on January 2, 1978. Because of recurrent cutaneous leg ulcers induced by trauma, warfarin was discontinued with marked improvement. Over the next few months, four trimethoprim-sulfamethoxazole daily were substituted for sulfisoxazole, azathioprine was increased to 150 mg per day and prednisone gradually decreased to 25 mg per day. Additional problems which responded to appropriate therapy included onycholysis of the fingernails and

TABLE 1

S.P. 6/21/76:
MAINE MEDICAL CENTER—CARDIAC CATHETERIZATION

Location	Heart Rate	Pressure MM HG		Mean
		Systolic	Diastolic	
AT REST				
RA	85		A = 11	6
RV	85	52	10	
MPA	85	52	28	37
PAW	85			28
AO	90	100	70	80
LV	90	100	10-36	
CARDIAC INDEX (L/MIN/M ²) = 2.1				
PULMONARY VASC. RESISTANCE (WOOD UNITS) = 4				
EXERCISE				
PAW	140			45
PA	140	87	44	65
CARDIAC INDEX = 4.3				
PULMONARY VASCULAR RESISTANCE = 3.5				

TABLE 2

STANFORD CARDIAC TRANSPLANTATION CRITERIA

1. Class IV cardiac disease, refractory to medical or surgical treatment, bed-chair existence, and/or poor prognosis for six to twelve month survival
2. Under age 50
3. Stable psychosocial history
4. Strong positive attitude on the part of the patient and his family after discussion of the transplant procedure and its risks
5. Adequate finances and medical insurance for pre-transplant evaluation
6. Availability of vigorous follow-up medical care when patient returns home

TABLE 3

STANFORD CARDIAC TRANSPLANTATION CONTRAINDICATIONS

1. Pulmonary hypertension with pulmonary vascular resistance of more than 8 Wood units
2. Active infection, especially pulmonary
3. Irreversible hepatic or renal disease
4. Other systemic disease such as malignancy, diabetes, symptomatic vascular disease
5. Recent pulmonary infarction unresolved on X-ray
6. Alcohol or narcotic dependency or abuse
7. History of psychiatric illness

TABLE 4

S.P. 6/3/77: MEDICATIONS

Daily Dose	
Prednisone	40 MG
Azathioprine	200 MG
Furosemide	200 MG
Triamterene	200 MG
KCl	40 MEQ
Dipyridamole	400 MG
Calcium Carbonate	1.6 GM
Warfarin	

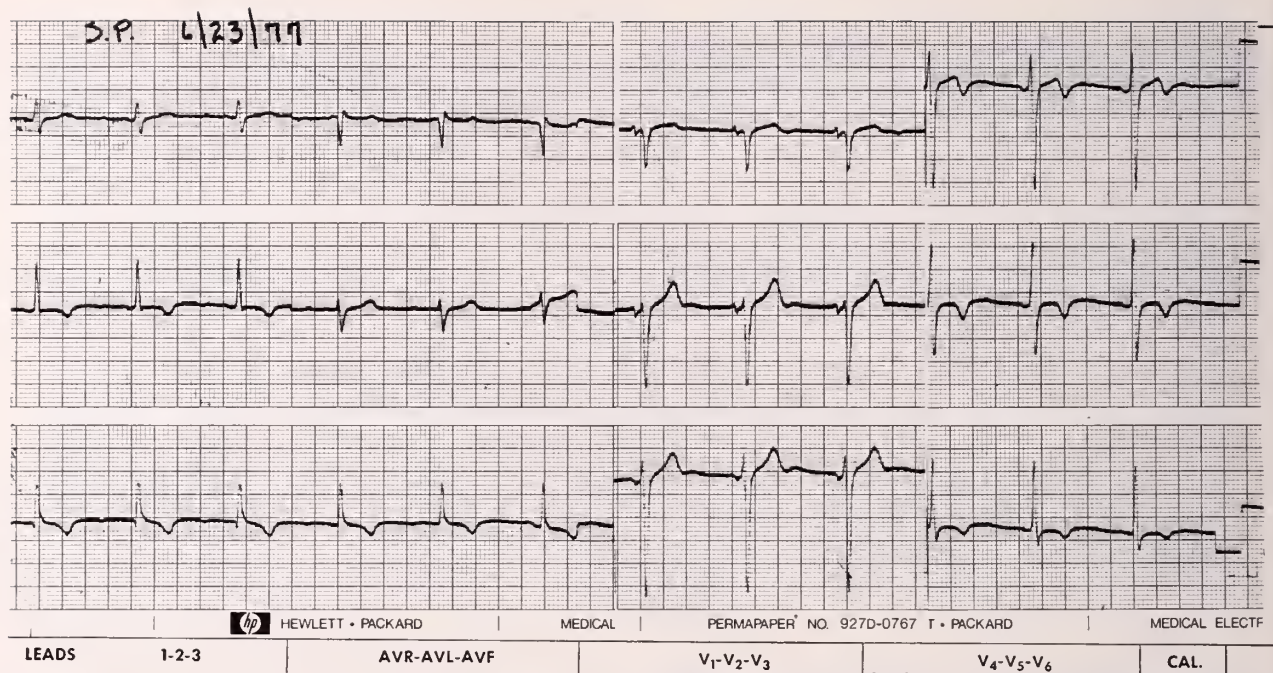


Fig. 1B. Postoperative Electrocardiogram.



Fig. 2B. Postoperative Chest Film.

monial pharyngitis. Second and third annual post transplant hemodynamic evaluations in February 1979, and February 1980, which included RV endomyocardial biopsies and coronary arteriography, were normal.

At present, more than three years following cardiac transplantation, S.P. experiences no cardiac symptoms, has had no further rejections or serious infections, and is a full-time college student. Medications are listed in Table 5. Current symptoms are related to chronic steroid and immunosuppressive therapy and include: bone pain due to aseptic necrosis of tarsal bones, skin fragility, and mildly impaired vision due to cataracts.

DISCUSSION

Since the first human cardiac transplant was performed in December 1967, by Barnard in South Africa, over 300 cardiac transplant operations have been performed in nearly two dozen countries. The operative technique is well described¹ and the large number of transplants performed in many centers in 1968 and 1969 following the initial success, reflects the relative ease of the operative procedure. However, difficulties in controlling rejection produced high mortality and the procedure has been discontinued in all but a few centers.

Currently in the U.S., cardiac transplantation is offered on a limited basis at S.U.N.Y. Downstate Medical Center, Brooklyn, Medical College of Virginia, Richmond, and Arizona Health Science Center, Tucson. The largest number of transplants in the world has been performed at Stanford University Medical Center, California, and recent reviews by Schroeder² and by Jamieson³ summarize their results through 1978. Through April 23, 1980, there were 75 survivors following 205 transplants in 188 patients.⁴ Stanford criteria for selection of patients are summarized in Table 2. Fifty-five percent of their recipients have had coronary heart disease and the remainder have had idiopathic, viral or rheumatic cardiomyopathy. Contraindications to transplantation are listed in Table 3.

Once a recipient is judged suitable for cardiac transplantation, the major problems are: donor supply, control of rejection, and control of infection. Other problems include: accelerated atherosclerosis, particularly of the coronary arteries, lipoprotein abnormalities, weight control, fluid retention, osteoporosis, cataracts, psychosocial adjustments and costs.

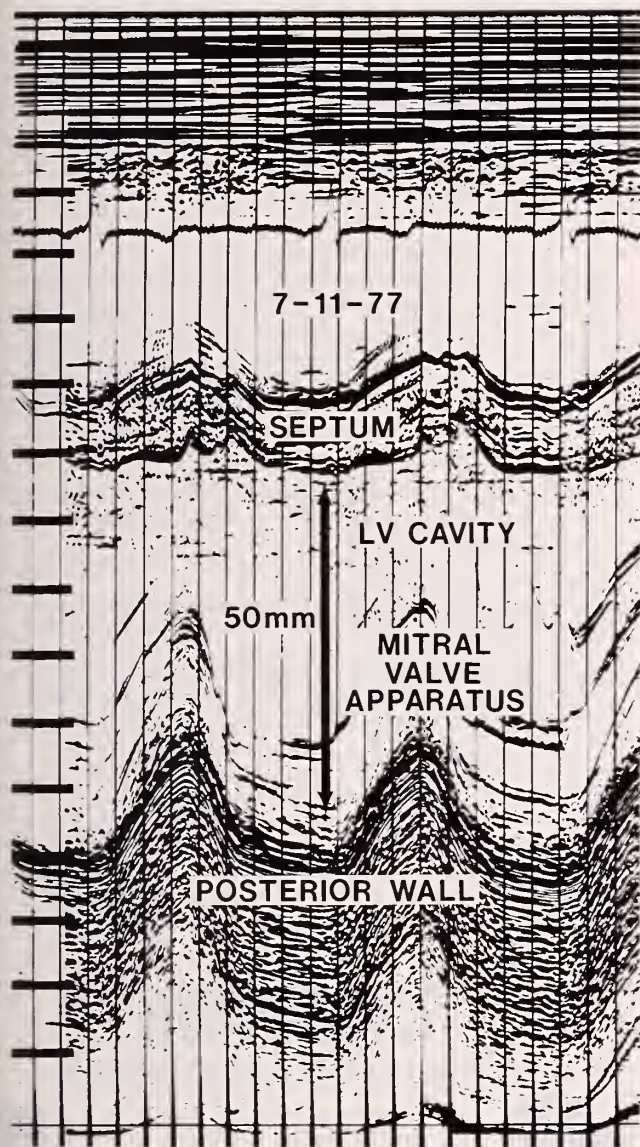


Fig. 3B. Postoperative Echocardiogram.

DONOR SUPPLY

Most donors at Stanford have experienced irreversible brain damage from trauma; the average age has been 27 years. There are three contraindications to the use of a donor for a particular recipient:¹ 1) ABO incompatibility, 2) positive crossmatch between recipient serum and donor lymphocytes, and 3) gross disparity in size of donor and recipient. A healthy donor heart is assured from detailed history and physical examination and by cardiac catheterization and coronary arteriography in men over 35 years and in women over 40 years. Recently, the donor supply has been increased with the use of isolated, cooled hearts transported and transplanted within three hours.

CONTROL OF REJECTION

Immunosuppression to prevent rejection following transplantation is accomplished by administration of rabbit antihuman thymocyte globulin (RATG), high

TABLE 5

S.P. APRIL 1980: MEDICATIONS

Daily Dose	
Prednisone	20 MG
Azathioprine	150 MG
Furosemide	160 MG
Triamterene	600 MG
Dipyridamole	400 MG
Calcium Carbonate	1.6 GM
Trimethoprim-Sulfamethoxazole	4 Tabs

doses of steroids and azathioprine before and after operation.⁵ Prednisone and azathioprine are continued lifelong; RATG is administered for 10 to 14 days after operation and thereafter as needed for actual or threatened rejection. Rejection is generally reversible with steroids in high doses although RATG may be required if rejection is severe. Uncontrolled rejection may require retransplantation which has been performed in 17 patients; there have been eight short-term survivors. S.P. developed signs of rejection three times: once acutely after transplantation which responded to steroids and RATG; again six months and again fifteen months following transplantation. Each episode responded to immediate, transient increases in prednisone to 100 mg daily.

CONTROL OF INFECTION

Patients with cardiac transplants are predisposed to infections because of the large doses of immunosuppressive agents given to prevent rejection. The infectious agents are frequently opportunistic organisms such as fungi, and S.P. developed a *Nocardia* lung abscess 6½ months following transplantation. Infections can be reduced by continuous administration of antibacterial combination agents, such as trimethoprim-sulfamethoxazole, which are administered routinely to all recipients unless contraindicated.

OTHER PROBLEMS

Accelerated coronary atherosclerosis may develop in some patients after transplantation, believed due to rejection-induced intimal injury.² Lipoprotein abnormalities from steroid administration may play a role, and transplant patients are given fat controlled diets. Coronary arteriography in S.P. three years after transplantation remains normal. Sodium restriction and diuretics are required to control fluid retention. Steroid administration also produces osteoporosis and aseptic necrosis, particularly of weight-bearing joints, as well as cataracts. S.P. is slightly limited by bone pain of ankle joints and notes mild visual impairment due to early cataracts. Patients referred for cardiac transplantation must be aware that: 1) they may be found unsuitable for transplantation; 2) a suitable donor may not be available despite serious deterioration in their condition; 3) life-threatening complications or death may occur following successful transplantation; 4) inten-

sive medical and drug therapy following transplantation are necessary and are accompanied by significant side effects and possible complications; and 5) significant psychosocial adjustment problems may occur. Psychosocial stability of the recipient is imperative and a supportive family clearly enhances overall recovery.

COSTS

In 1978, the average cost for the first year of cardiac transplantation at Stanford was approximately \$50,000, and subsequent yearly costs for medication and medical care were estimated at \$2,300. Obviously, these costs have increased substantially in two years. About half of these costs are covered by insurance carriers. Costs of traveling to and from Stanford, all costs of initial evaluation as an out-patient, and any hospitalization or medical care prior to actual transplantation must be assumed by the patient. Costs of the transplant operation and after care while at Stanford Hospital, not covered by patient's insurance, may be covered by a government grant. Expenses after the patient has returned home are not so covered, however. There are no provisions for financial aid for living costs in the Palo Alto area for the patient and his family while being evaluated for or awaiting transplantation. The average waiting period once the patient has been accepted for transplantation is three months and this may be longer, depending upon availability of a donor.

SURVIVAL

Survival following cardiac transplantation at Stanford has improved steadily with a current one-year survival of 70 percent and an annual attrition rate of 5 percent. In 94 consecutive patients undergoing transplantation between 1973 and February 1979, the survival rates at Stanford were: one year: 63 percent; two years: 58 percent; three years: 54 percent; four years: 54 percent.⁵ These results are comparable to graft survival rates in patients with renal failure who have received cadaver renal transplants. The successful cardiac transplantation program at Stanford is a result of many factors: continued research and development of techniques for patient management and control of rejection and infection; total commitment of teams of cardiac surgeons, research workers, cardiologists, nurses, and social workers; and a more than ten-year experience with the unique problems of cardiac transplantation.

Despite problems which include supply of donor hearts, costs, transplant rejections and complications the current survival rate of 70 percent and functional rehabilitation in 90 percent of recipients indicate the effectiveness of cardiac transplantation. Therefore, this procedure should be considered in selected patients with end stage heart disease.

Cardiac transplantation was clearly lifesaving in the patient described in this report, and death would surely have occurred within a few weeks had not transplantation been performed. He must take many

tablets and capsules daily, restrict fluid and salt intake, and undergo detailed medical checkups every few weeks. He experiences ankle pain, skin fragility, and mildly impaired vision. Nevertheless, this young man is alive more than three years after successful cardiac transplantation, enjoys an active and useful life, and is optimistic about his future.

ACKNOWLEDGMENTS

Appreciation is expressed to: John S. Schroeder, M.D. (Cardiology Division) and Stuart W. Jamieson, M.D. (Dept. of Cardiovascular Surgery) of Stanford University Medical Center for providing invaluable information in the preparation of this report; to Joanne Nelson and Swan Colpitts for preparation of the manuscript; and to Douglas MacKenzie for preparation of the photographs.

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Management of the Injured Spleen Without Splenectomy

DAVID E. CLARK, M.D.* AND MICHAEL R. CURCI, M.D.*

For half a century, splenectomy has been the standard treatment for any injury to the spleen, and thousands of lives have been saved by this rapid and effective operation. However, several recent studies have established a small but significant increased incidence of overwhelming infection after removal of the spleen, especially in children.¹⁻³ Management of the injured spleen without splenectomy has become common practice in pediatric surgery and is now being applied to older patients as well.^{4,5}

CASE REPORTS

Since 1974, twelve patients admitted to the Maine Medical Center with evidence of splenic injury have been managed either by observation or by splenorrhaphy (Table 1). This group includes most of the children with splenic trauma during this period, and an increasing number of adults. However, the great majority of adults are still being treated with splenectomy.

Five patients with a clinical suspicion of splenic injury confirmed by Technetium-99m sulfur colloid scan were observed for 4-13 days in the hospital without paracentesis or laparotomy. Repeated physical examinations and hematocrits were performed. The patients were kept at bed rest, with nasogastric suction and nothing by mouth until symptoms resolved and peristalsis returned. One patient required a single transfusion because of a low hematocrit. All recovered and subsequently had normal spleen scans.

One boy (Case 1), who was successfully treated in this manner, suffered another blunt injury four years later (Case 6). Radionuclide scan (Figures 1-4), which had shown healing of the previous injury, now revealed evidence of a new laceration. He was again admitted and observed, but because of progressive signs of peritoneal irritation during the initial 24 hours, he underwent exploratory laparotomy. The spleen was found to be completely transected; its ischemic upper half was resected, while successful repair of the viable lower half was accomplished.

In five other patients, splenic injury encountered at laparotomy was repaired, preserving most of the spleen. In each case, a thorough abdominal exploration and complete mobilization of the spleen preceded any attempt at splenorrhaphy. Contused or ischemic portions were excised and hemostasis of raw edges or lacerations was achieved using mattress or figure-eight sutures of chromic catgut. Bleeding points were further controlled with clips, sutures, or microfibrillar collagen hemostat (Avitene, Avicon Inc.) Small pedicles of omentum were used in several cases as pledgets or bolsters to provide further hemostasis. All patients recovered and were discharged without complications one to three weeks postoperatively. Hospitalizations over ten days were due to associated renal or orthopedic injuries.

In addition to the cases in Table 1, another 20-year-old man has recently had a successful splenorrhaphy but is still hospitalized because of a head injury. In two other patients, splenic repair was attempted without success, and splenectomy was performed. One of these patients was noted to have an enlarged and very friable spleen and postoperatively mononucleosis was diagnosed by serologic test and microscopic examination of the specimen.

One patient (Case 10) presented with an abdominal mass which

had been palpable and growing slowly for at least five years. The patient and her mother recalled a blunt injury to the left upper quadrant from her bicycle handlebar when she was struck by a car as a child. Radionuclide and CAT scans demonstrated a large splenic cyst, which was confirmed at laparotomy. After complete mobilization of the spleen, the cyst was excised with the attached upper pole of the otherwise normal spleen, and hemostasis was obtained using the methods described above. Pathologic examination revealed a typical post-traumatic pseudocyst containing three liters of brownish fluid.

DISCUSSION

Our experience at the Maine Medical Center confirms that splenic injury can be safely managed in selected patients without splenectomy. There were no complications, but it is possible that Case 6 was more susceptible to injury because of his previous trauma. Although complications of nonoperative management have not yet been reported, the theoretical risks are delayed bleeding, pseudocyst or abscess formation, and failure to identify associated injuries. Partial splenectomy or splenorrhaphy may also be followed by late hemorrhage, as exemplified by a recently published case.⁶

Management of splenic trauma without exploratory laparotomy is controversial even among pediatric surgeons, but has been practiced by surgeons at the Hospital for Sick Children in Toronto for 35 years.⁷ Their method, which we have used with modifications, includes observation in an intensive care setting for at least 24-48 hours, with nasogastric suction "until gastrointestinal function returns and the abdomen is soft and nontender." Transfusions are given as needed, and hospitalization may last two to three weeks in an uncomplicated case. Clinical instability, evidence of continuing hemorrhage, or suspicion of associated intra-abdominal injury mandate exploratory laparotomy.

The development of various techniques of splenorrhaphy has been reviewed and illustrated by Buntain and Lynn,⁵ and similar principles in the management of splenic cysts have been employed by Morgenstern and Shapiro.⁸ The growing number of case reports, and our own experience, demonstrate that the spleen can be successfully repaired. However, if the time necessary for splenorrhaphy will delay the management of other critical injuries, or if hemostasis after splenorrhaphy is insecure, splenectomy should be performed without compunction.

Attempts to avoid splenectomy have been stimulated by an improved understanding of the immunologic importance of the spleen. Sepsis occurring after splenectomy, usually due to the pneumococcus, is characterized by a rapidly progressive course, with disseminated intravascular coagulation, peripheral cyanosis, and purpura.^{2,3} Three episodes in two adult

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Fig. 1



Fig. 2

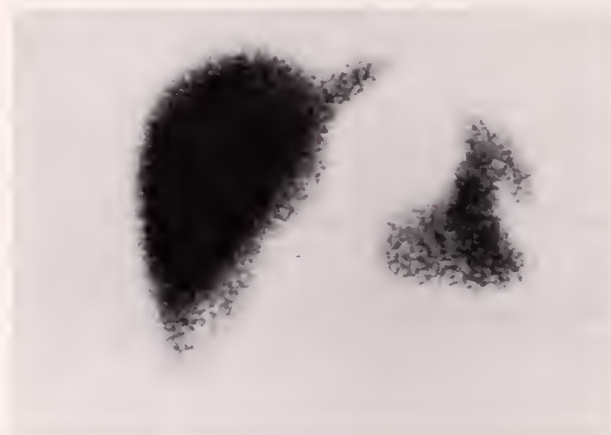


Fig. 3



Fig. 4

Figures 1-4: 1) 9/20/74 Technetium-99m sulfur colloid scan showing injury to upper pole of spleen and left lobe of liver (Case 1). 2) 1/17/75 Scan showing healed spleen and liver. 3) 4/15/78 Scan of same patient showing transverse laceration of spleen (Case 6). 4) 10/4/78 Scan showing healing and regeneration of spleen.

patients have been treated at the Maine Medical Center within the last five years (Table 2). One patient recovered from her first attack, only to die despite aggressive treatment of a recurrence ten months later. The other patient has recently been discharged after a stormy course; amputation of gangrenous toes was required. A collective review by Kingston and MacKenzie revealed a mortality of over 90% in adults with this syndrome, and found reports of only three similar patients with normal spleens in the world literature (two in Polish, one in Romanish).³

The incidence of overwhelming sepsis following splenectomy is controversial, since many patients undergoing splenectomy have underlying hematologic or neoplastic diseases which may also predispose to infection. Only 21 cases with severe sepsis after splenectomy for trauma have been published,⁹ but the majority are probably not reported. Using gross statistical methods, Singer² estimated that 0.58% of patients undergoing splenectomy for trauma will subsequently die of sepsis, compared to 0.01% of the normal population. Since the

experience of any one center is minimal, long-term cooperative studies will be needed to clarify the true incidence of infection following splenectomy.

Since the original report of sepsis in infants undergoing splenectomy for congenital spherocytosis,¹⁰ the risk has been ascribed primarily to the youngest age groups. However, if splenectomy for hematologic disease is eliminated, small children are no longer the most frequent victims of overwhelming infection. Singer² found that most published cases of sepsis following splenectomy for trauma occurred under the age of 15, but that the ages ranged from 6 to 46. Overwhelming pneumococcal infection has occurred as long as 27 years after splenectomy,⁵ and has been increasingly recognized as a consequence of splenectomy in adults as well as children.³

Pneumococcal sepsis after splenectomy is most often fatal even with aggressive treatment. Prophylactic penicillin may reduce the chance of infection, but compliance with prophylactic regimens is notoriously poor. Infections have been reported due to penicillin-resistant organisms.¹¹ The available pneumococcal vaccines (Pneumovax[®], MSD; Pnu-

TABLE 1

PATIENTS WITH SPLENIC INJURY SUCCESSFULLY MANAGED WITHOUT SPLENECTOMY						
Case	Year	Age/Sex	Cause	Diagnosed	Management	Hosp. Days
1*	1974	5/M	Fall/bike	Scan	Observation	8
2	1976	5/M	Fall/tractor	Lap	Splenorrhaphy	17
3	1977	5/M	Auto/pedes.	Scan, Lap	Splenorrhaphy	19
4	1977	7/F	Auto/pedes.	Tap, Lap	Splenorrhaphy	12
5	1977	17/M	Fall	Scan	Observation	4
6*	1978	9/M	Skiing	Scan, Lap	Hemisplenectomy	9
7	1978	11/F	Fall/bike	Scan	Observation	13
8	1979	16/M	Auto	Scan	Observation	10
9	1980	20/M	Auto	Tap, Lap	Splenorrhaphy	22
10	1980	21/F	Auto/bike**	Scan, Lap	Exc. Pseudocyst	8
11	1980	15/M	Hockey	Lap	Splenorrhaphy	8
12	1980	16/F	Auto	Scan	Observation	8

*Same patient

**Remote injury

TABLE 2

PATIENTS WITH POSTSPLENECTOMY PNEUMOCOCCAL SEPSIS					
Case	Year	Age/Sex	(Age at splenectomy, reason for splenectomy)	Hospitalization	Outcome
1*	1975	27/F	(19, splenic cyst)	10 days	Recovered
2*	1976	28/F	(19, splenic cyst)	6 hours	Died**
3	1980	40/M	(38, lymphoma)	97 days	Recovered

*Same patient

**Adrenal hemorrhages at autopsy

immune, Lederle) cover only the most common serotypes, and infection can occur even with serotypes covered by the vaccine.^{12,13} Accessory spleens, splenosis, or surgically reimplanted splenic remnants may provide some protection, but this is incomplete and possibly insignificant.¹⁴ To date, sepsis has not been reported in any patient who has had successful repair or nonoperative management of an injured spleen.

CONCLUSION

Management of the injured spleen without splenectomy in selected children and adults is safe and is justified to prevent catastrophic infection later in life. Pneumococcal sepsis after splenectomy for trauma is uncommon, but it is not limited to children and is usually fatal. Although splenectomy is still an appropriate and lifesaving operation in many cases of splenic injury, we believe the spleen should be preserved whenever possible.

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Esophageal Perforation

Some Guidelines for Diagnosis and Management

CLEMENT A. HIEBERT, M.D.*

INTRODUCTION

When it comes to sheer woe, a hole in the esophagus is trouble in a class by itself—trouble from:

- 1.) Not recognizing the perforation promptly
- 2.) Not managing it properly
- 3.) Making it in the first place

Causes of esophageal disruption are numerous and include: instruments, sharp objects, and necrotizing fluids pushed or swallowed from above, projectiles, sutures, and instruments lacerating from the side, and gastric fluid erupting from below. This paper will deal with 1.) so-called spontaneous rupture and 2.) perforation from instrumental misadventure.

I. "SPONTANEOUS" RUPTURE: A flagrant misnomer suggesting an insidious and nonviolent occurrence. A better term is needed for this highly lethal *explosion* of gastric ferment and food into the mediastinum and left pleural space, classically the result of forceful or suppressed vomiting following a prodigious meal or alcoholic debauch. It is by no means rare.

Diagnosis: The pain is sudden, unremitting, and of such intensity as to be unrelieved by ordinary doses of opiates. It is felt deep in the precordial and epigastric areas, is worsened by movement, and accompanied by tachypnea, cyanosis, and progressive hypotension. Suprasternal crepitus is an inconstant sign, but spasm of the upper abdomen is usual and, because of it, the general surgeon may be early on the scene.

When a doctor examines a patient with acute abdominal pain, one of the first things he considers is the possibility of inflamed or perforated intestine. When the doctor examines a patient with severe *chest* pain, however, a hole in the esophagus is the *last* thing considered. While meditating on the possibilities of perforated ulcer, pancreatitis, myocardial infarction, pulmonary embolism, and dissecting aneurysm the golden opportunity to operate in a relatively uninflamed field is lost; mediastinitis, empyema, starvation, are among the appalling array of complications which result in death in well over 50% of cases diagnosed after 24 hours.

The essential clue is chest pain *following* vomiting and the clincher is a Gastrografin® swallow and an upright chest film showing gas and fluid in the mediastinum and left pleural space.

Treatment: In contrast to almost certain death if the condition goes unrecognized, up to 92% of patients may survive with proper care. Even so, complications are the rule.¹ Goals of treatment include: 1.) *Control of inflammation* with antibiotics, debridement, and drainage tubes. 2.) Fluid and *nutritional maintenance* via large vein alimentation. 3.) Construction of a *dehiscence proof suture line* is the *sine qua non* and is predictably possible only when patched with stomach, diaphragm, omentum, etc. Girdling of the esophagus with a pedicle of pleura is a promising contribution of Grillo and Wilkins.² 4.) *Isolation of the esophageal mucosal wound* from saliva and gastric juices. 5.) *Correction of antecedent conditions:* Chronic incompetency of the lower esophageal sphincter may predispose to postemetic tears³ by; a.) facilitating the flood of gastric contents necessary to rupture the gullet and b.) initiating the catastrophe with reflux irritation of the esophagus. The Mark IV technique of Belsey buttresses the suture line, prevents gastric fluid from corrupting the mucosal aspect of the repair, and eliminates what occasionally may be the primary disorder, viz, chronic reflux and vomiting.

II. INSTRUMENTAL PERFORATION: It remains a sobering fact that most esophageal injury is caused by doctors. The incidence of esophageal perforation consequent to abdominal vagotomy is one in two hundred operations⁴ and is in the same order of magnitude as endoscopic perforation.⁵

Hazards of esophagoscopy include: 1.) The combination of a rigid scope, prominent incisor teeth, and a stiff neck. 2.) Cervical vertebrae with spurs. 3.) Mistaking the neck of a diverticulum for the main channel. 4.) Forceful advancement of any instrument. 5.) Inoculation of the mediastinum with anerobes originating in peridental sepsis. 6.) Inadequate patient cooperation, relaxation, or sedation. 7.) Use of an endotracheal tube with an inflated cuff. 8.) Inexperience and lengthy examination.

Even with due care the esophagus can easily be injured, particularly at the level of the cricopharyngeus or near tumor, stricture, or a foreign body. Substantial pain with dysphagia, or crepitus alone are indications for a Gastrografin swallow with frontal and lateral views of neck and chest.

While tiny defects can doubtless be managed conservatively, an argument can also be made for closing all perforations as neither the size of the hole nor the

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Cardiac Surgery in the Elderly

EDWARD R. NOWICKI, M.D.,* CHRIS A. LUTES, M.D.* AND RICHARD L. WHITE, M.D.*

Cardiac surgery in the elderly can be performed with an acceptably low mortality and a high probability for improved quality of life after surgery.^{1,2} While heart surgery in older patients is a challenge, the age factor alone is not the most important determinant of risk. Rather, cardiac failure prior to surgery is the main risk in these patients.³ This report presents our experience with cardiac surgery in elderly patients and emphasizes the operative mortality and the postoperative morbidity.

CLINICAL MATERIAL

Eight-hundred patients were operated on by the authors at the Maine Medical Center, using cardiopulmonary bypass, to correct various cardiovascular problems from January 1977 to January 1980. Eighty (10%) of these patients who were 70 years of age or older form the basis of this report. The age range was 70 to 83 years (74 average). There were 43 (54%) men and 37 (46%) women. Cardiac catheterization or aortography was performed on all patients prior to surgery. Myocardial protection was achieved in nearly all patients by systemic cooling to 22 to 28 degrees C, topical cold saline irrigation of the heart, and cold potassium cardioplegia. Hemodilution with a bloodless oxygenator prime was used for most patients. Where safe, 500 ml of blood were removed from the patient immediately prior to bypass and reinfused at the end of the procedure.

Elective operations were performed on 76 patients with 2 deaths (2.6%). Three (75%) of four patients undergoing emergency operation died. The overall mortality rate was 6.3% (5 of 80 patients). Thirty coronary artery bypass procedures were performed on 30 patients with 1 death (3.3%). Aortic valve replacement was performed on 21 patients and mitral valve replacement on 11 patients with no deaths. Combined procedures were performed on 15 patients with 2 deaths (13%). One patient with ruptured ventricular septum due to myocardial infarction survived operation. Two deaths occurred in two patients operated on for dissecting hematoma of the aorta (Table 1).

RESULTS

In the 30 patients who had coronary artery bypass surgery only, 11 (35%) had left main trunk obstruction of more than 50% of the lumen. Four (36%) of these 11 patients with left main trunk lesions had unstable angina, similar to the incidence of unstable angina in the entire group of 30 patients which was 39% (12 patients). Myocardial infarction had occurred previously in 14 (45%) of these 30 patients.

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TABLE 1

CARDIOVASCULAR SURGERY IN PATIENTS 70 YEARS AND OLDER				
	Number		Deaths	
CABG 1	1			
2	6 (1)*			
3	11			
4	8			
5	4			
	30	30	37.3%	(1)*
AVR		21	26.2%	
MVR		11	13.6%	
AVR & CABG 1	6 (1)			
2	2			
3	1			
4	1			
	10	10	12.3%	(1)
CABG 3 & Mitral Valvotomy	1		1.2%	
MVR & CABG 2	1		1.2%	(1)
LV Aneurysm Resection				
CABG 2	1		1.2%	
AVR & MVR & CABG 1	1		1.2%	
MVR & Tricuspid Annuloplasty	1		1.2%	
Repair Ruptured Ventricular Septum	1		1.2%	
Attempted Repair Dissecting Aneurysm	1		1.2%	(1)*
Repair Dissecting Aneurysm	1		1.2%	(1)*
	80	100.0%		(5) (6.3%)

*Emergency Operation

CABG = coronary artery bypass graft; AVR = aortic valve replacement; MVR = mitral valve replacement; LV = left ventricle

TABLE 2

POSTOPERATIVE COMPLICATIONS CORONARY ARTERY BYPASS (29 SURVIVING PATIENTS)		
	Patients	
Re-op Bleeding	4	15%
Re-op Sternal Dihiiscence	3	10%
Stroke	0	0%
Temporary Post-op Psychosis	8	28%
Supraventricular Arrhythmia	11	38%
Ventricular Arrhythmia	2	7%
Atelectasis	15	53%
Bronchospasm	3	10%
Congestive Heart Failure	5	17%
Significant Myocardial Injury	2	7%
Low Cardiac Output Post-op (IABP)	1	3%

IABP = Intra-aortic balloon pump

The ejection fraction was measured in 21 patients and averaged 63% (range 32 to 81%). The average postoperative stay was 13.6 days (range 6-25 days). Table 2 lists postoperative complications.

In the 21 patients who had aortic valve replacement only, the NYHA functional class data were known in 19. Three (16%) were in Class 2, 15 (79%) in Class 3 and 1 (5%) in Class 4. Three (14%) of the 21 patients had angina. Fourteen (93%) of fifteen

TABLE 3

**POSTOPERATIVE COMPLICATIONS
AORTIC VALVE REPLACEMENT (21 PATIENTS)**

	<i>Patients</i>	
Re-op Bleeding	1	5%
Re-op Sternal Dehiscence	1	5%
Stroke (mild paresis)	2	10%
Temporary Post-op Psychosis	2	10%
Supraventricular Arrhythmia	11	53%
Ventricular Arrhythmia	1	5%
Atelectasis	10	48%
Congestive Heart Failure	7	33%
Perioperative MI	1	5%
Low Cardiac Output Post-op	0	0%

MI = myocardial infarction

TABLE 4

**POSTOPERATIVE COMPLICATIONS
MITRAL VALVE REPLACEMENT (11 PATIENTS)**

	<i>Patients</i>	
Re-op Bleeding	0	0%
Re-op Sternal Dehiscence	0	0%
Stroke	0	0%
Temporary Post-op Psychosis	1	10%
Supraventricular Arrhythmia	2	20%
Ventricular Arrhythmia	3	27%
Atelectasis	5	45%
Congestive Heart Failure	3	27%
Perioperative MI	0	0%
Low Cardiac Output Post-op	0	0%

MI = myocardial infarction

who had coronary arteriograms had no obstructive coronary artery disease. One patient had single vessel disease with 40-50% luminal stenosis. The ejection fraction measured in 15 patients averaged 58% (30-83%). The aortic valve gradient in 17 patients averaged 105 mm Hg (50-175 mm Hg). Aortic stenosis without significant aortic regurgitation occurred in 17 (81%) of the 21 patients. Only 2 (10%) of the 21 patients had pure aortic regurgitation as the indication for aortic valve replacement. In 4 the valve was replaced with a Bjork-Shiley® prosthesis. Porcine heterograft valves were used in the remaining 17 (81%) of the patients. The average postoperative stay was 16.4 days (range 9-46 days). Postoperative complications are listed in Table 3.

All patients who had mitral valve replacement were in functional Class 3 or 4. Eight (72%) of the 11 patients had moderate or severe mitral regurgitation. Most had significant mitral stenosis as well. All ejection fractions measured were over 45%. Porcine heterograft valves were used in 9 (82%) patients and Bjork-Shiley valves in the remaining 2 (18%) patients. The average stay after surgery was 16.3 days (range 10-28 days). Postoperative complications are listed in Table 4.

Of the 15 patients who had combined procedures, 10 had aortic valve replacement and coronary artery bypass grafting. Eight (80%) of these, 10 patients

Continued on Page 277

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Brief Summary

INDICATION Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect, rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. **Drug Dependence.** Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy:* Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children:* Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache, rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomeastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg tablet three times daily, one hour before meals, and in mid evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg tablet daily, swallowed whole, in midmorning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdose include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdose.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.
Cayey, Puerto Rico 00633

Direct Medical Inquiries to
MERRELL-NATIONAL LABORATORIES
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Licensor of Merrell®

References: 1. Citations available on request from Medical Research Department, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga, M. T., O'Dillon (Dillon), R. H., and Leyland, H. M. A comprehensive review of diethylpropion hydrochloride. In: *Central Mechanisms of Anorectic Drugs*, S. Garattini and R. Samanin, Ed. New York, Raven Press, 1978, pp. 391-404.

Merrell

TABLE 5

POSTOPERATIVE COMPLICATIONS AORTIC VALVE REPLACEMENT AND CORONARY ARTERY BYPASS (10 PATIENTS)		
	Patients	
Re-op Bleeding	3	30%
Re-op Sternal Dehiscence	0	0%
Stroke	0	0%
Temporary Post-op Psychosis	1	10%
Supraventricular Arrhythmia	2	20%
Ventricular Arrhythmia	0	0%
Atelectasis	4	40%
Bronchospasm	1	10%
Congestive Heart Failure	2	20%
Significant Myocardial Injury	1	10%
Low Cardiac Output Post-op	1	10%

TABLE 6

DEATHS	
<i>Elective Operations</i>	<i>Causes of Death</i>
AVR & Single CABG	Myocardial Infarction
	Low Cardiac Output
MVR & Double CABG	Severe generalized bleeding
<i>Emergency Operations</i>	
Double CABG	Pre-op myocardial infarction
Attempted repair Type I	Inability to control aortic
Aortic Dissection	tear
Repair Type III	Stroke
Aortic Dissection	

AVR = aortic valve replacement; CABG = coronary artery bypass grafting; MVR = mitral valve replacement

were in functional Class 3 and 2 (20%) were in Class 4. Four (40%) of the 10 patients had angina. One patient had a left main trunk stenosis greater than 50% of the lumen. The ejection fraction measured in eight patients averaged 50% (range 17-68%). The aortic valve gradient in 8 patients averaged 90 mm Hg (56-136 mm Hg). Two (20%) of the 10 patients had severe aortic regurgitation. Eight patients had porcine heterograft valves and 2 had Bjork-Shiley valves. The average stay after surgery was 13 days (range 10-22). Table 5 lists postoperative complications.

The remaining 5 combined procedures were as follows: 1) a patient in functional Class 4 with angina who had aortic and mitral valve replacement plus single coronary artery grafting, 2) a patient with mitral stenosis and limiting angina who had triple coronary artery grafting and mitral valvotomy, 3) a patient in functional Class 4 with severe mitral stenosis and tricuspid regurgitation who had mitral valve replacement and tricuspid annuloplasty, 4) a patient with unstable angina and heart failure who had resection of a left ventricular aneurysm and double coronary artery grafting, and 5) a patient (functional Class 4) with mitral stenosis and angina due to double vessel disease who had mitral valve replacement and double coronary artery grafting.

There were 2 deaths in patients operated on elec-

tively. One woman aged 73 years had aortic valve replacement and single coronary artery bypass grafting. She was in functional Class 4 with aortic stenosis, a 100 mm Hg aortic valve gradient, a left ventricular end diastolic pressure of 35 mm Hg, an ejection fraction of 17%, and a right coronary artery stenosis unrecognized at catheterization. Following aortic valve replacement alone, the right ventricle did not function well when coming off cardiopulmonary bypass. Right coronary artery bypass grafting was done during another short period of cardiopulmonary bypass. The total ischemic interval was 65 minutes and the total bypass time 150 minutes. Although the patient was weaned from cardiopulmonary bypass with the intra-aortic balloon pump and inotropic agents, she died 48 hours later of myocardial infarction with low cardiac output. Another woman aged 72 years, who died after elective operation, had mitral valve replacement and double coronary artery grafting for severe mitral stenosis with regurgitation (functional Class 4) and angina with previous myocardial infarction. The total bypass time was 125 minutes with no difficulty coming off cardiopulmonary bypass, but severe generalized bleeding could not be controlled in the operating room and she died.

Among the 3 patients who had emergency operations and died were two patients with dissecting hematoma of the aorta. The first man aged 70 had a Type I aortic dissection with cardiac tamponade, anuria, and ischemic gut and died in the operating room when attempts to control the aortic tear were unsuccessful. The second patient, a man aged 75 years, died 32 days after successful repair of a Type III aortic dissection due to a stroke, pneumonia, and sepsis. The third patient who died in the emergency group was a 78-year-old woman with unstable angina, a previous myocardial infarction, and an ejection fraction of 42%. She suffered acute myocardial infarction hours before surgery and had a pulmonary capillary wedge pressure of 25 mm Hg at the time of induction of anesthesia. In spite of complete revascularization, the patient could not be weaned from cardiopulmonary bypass Table 6.

DISCUSSION

Poor cardiac function is the greatest cause of increased surgical risk in elderly cardiac surgery patients, not age per se or associated diseases.^{1,3} Myocardial infarction and low cardiac output superimposed upon already diminished cardiac reserve are the most common factors that lead to postoperative death in these patients.^{5,6} The incidence of myocardial infarction in our group of older patients was 5% and the mortality rate in the overall series was 6.3%, 2.6% in elective cases. Others have reported a 3.7% to 17% mortality rate in the elderly age group having heart surgery.^{1,5}

Several factors are important in minimizing myocardial injury during heart surgery. The recognition and concomitant surgical treatment of significant

coronary artery disease in patients who require valve surgery is important. Others have shown this to be true. Indeed, long-term survival may be enhanced.^{7,8,9} In our series of patients, none of the 32 patients who had isolated aortic or mitral valve replacement died. Nearly all of these patients had coronary arteriography which demonstrated no significant obstructive disease (greater than 50% stenosis of the lumen). One of these patients had a myocardial infarction following surgery but survived without low cardiac output. Of the 10 patients who had combined aortic valve replacement with coronary artery bypass grafting, one patient died of myocardial infarction with low cardiac output. An undiagnosed tight stenosis of the right coronary ostium in this patient was responsible for operative myocardial injury and death.

Another important factor which influences the morbidity and mortality in cardiac surgery patients is the success of myocardial protection by cold potassium cardioplegia during periods of induced operative ischemia.¹⁰ To protect the myocardium, all of the patients in this series were cooled systemically to 22° to 28°C and the coronary arteries perfused with cold (4°C) potassium arrest solution.

Some of the factors which relate to morbidity in the postoperative period are ease of mobilizing the patient and degree of cardiac failure and arrhythmias prior to operation. There is more difficulty ambulating the older patient. Long-standing cardiac failure before surgery is not always reversed promptly in the immediate postoperative phase as our experience shows. Cardiac arrhythmias frequently persist postoperatively and require intensive medical treatment. Others have reported similar findings and an average postoperative stay of 28 days in cardiac surgical patients 65 and older.^{6,3} The postoperative stay in our series of older patients averaged 14 days, in contrast to 7-10 days for younger patients having coronary artery surgery and 8-14 days for those having valve replacement.

Life expectancy is increasing. A person who reached age 65 in 1970 had an average remaining lifetime of 15 years.⁴ Because of increased longevity, more

aged patients with surgically treatable heart disease will be considered for cardiac surgery in the future.

In summary, our experience with cardiac surgery in patients 70 and older at Maine Medical Center supports what has been published recently in the literature. Older patients can have cardiac surgery with low risk. Identification of significant associated coronary artery disease and its treatment at the time of surgery in patients with valve disease decreases the chance of postoperative myocardial infarction and death. Further improvement in operative mortality and decrease in postoperative morbidity in the older age group will likely come from earlier operation before cardiac functional reserve is depleted.

ACKNOWLEDGMENTS

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CME in Maine

Refer to August issue, pages 257-259

WATCH FOR NEW LISTINGS IN OCTOBER ISSUE

Diagnostic Imperatives in Internal Medicine

The Timely Detection of Treatable Disease

Cancer

MARY E. COSTANZA, M.D.*

INTRODUCTION

By its nature, cancer presents serious problems for the practitioner dedicated to definitive or curative intervention. Cure of the solid tumor means, with few exceptions, eradication of localized disease (see Table 1). Permanent control of solid cancers is generally accomplished by surgical excision or occasionally by small field radiotherapy. Chemotherapy or systemic drug therapy is, on the whole, an unsuccessful curative method. Yet, discovering truly small cancers is a frustrating exercise, as screening procedures yield too many benign lesions and hardly any curable cancers.

I. BLIND SCREENING

The very smallness of the curable lesion precludes its easy discovery. Small lesions have little or no direct mass effects and few if any indirect "humoral" ones. They are the truly silent, but curable lesions, if only they could be found in time. In the past, this tantalizing promise of cure prompted many into launching comprehensive screening programs of asymptomatic people. But the overall poor results of broad cancer screening programs have dampened almost everyone's spirits. Screening a symptomless population results in the detection of too few early cancers and too many false "lesions."

Why does this particularly frustrating state of affairs exist? The typical curable cancer at the time of detection might be about 1 cm. in diameter, containing as many as 1 *BILLION* cells. Surprisingly, most screening, palpation or radiographic techniques do not consistently discriminate lesions at much below this size. Because many tumor cells do make specific "tumor" identifiable products, searching for diagnostic tumor products has seemed a more hopeful method of cancer detection. Unfortunately, as it has become clearer with successive screening programs, these tumor products or markers are usually present in too low a concentration to be detected at a time when the cancer is still curable. Typically, tumor markers become diagnostic at a point where no competent physician need use them, for example, when the liver is full of metastases. The difficulty expressed in the unreliability of tumor markers reflects the basic problems inherent in biologic tests. If a test is sensitive enough to pick up small tumors, it is usually not specific enough. Conversely, if specific enough,

TABLE 1

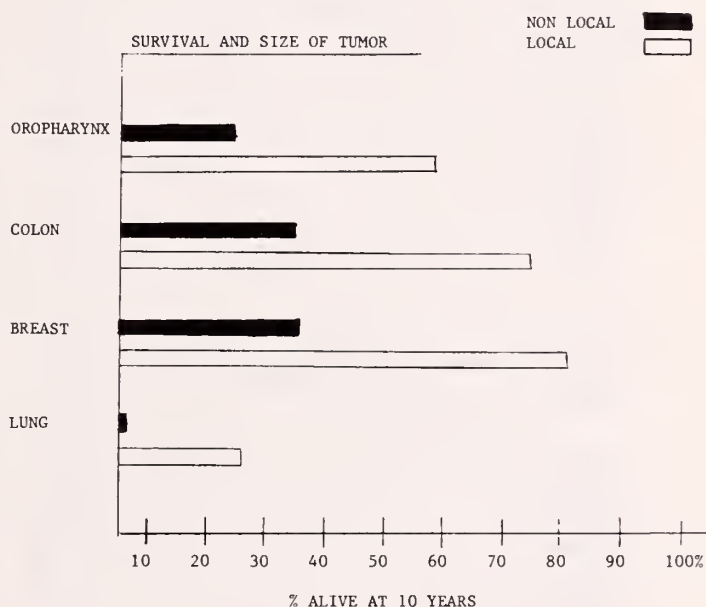


TABLE 2

A TYPICAL SCREENING CANCER TEST

Suppose a test yields 10% false-positives, and 80% false-negatives for early cancer

Suppose in screening a population of 100,000 over 40 years old, there will be 50 cancers

Suppose there will be 25 early cancers; and 25 late cancers

For every 100,000 tests done:

10,000 will be false-positive

37 true-positive (12 early cancers found in this group)

13 false-negative (13 early cancers missed)

Therefore, 100,000 tests will yield only 12 early cancers, but will require 10,000 unnecessary further workups on the false-positive patients.

[This is approximately the end result of CEA screening for colorectal carcinomas!]

then it is usually insensitive to early disease. For example, even if a blood test were 90% accurate, it would still be ineffective since the vast majority of the subjects screened do not have cancer (see Table 2).

If mass screening of a symptomless population is an unfeasible way to find curable cancer, is there anything else to be done? Should we wait until the patient presents with some suspicious symptom? Table 3 emphasizes the disparity in presentation for

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TABLE 3

PERCENT OF CASES DIAGNOSED AT VARIOUS STAGES			
Organ	Local	Regional	Distant
Lip	84%	10%	4%
Tongue	41	35	20
Mouth	44	37	15
Pharynx	20	49	27
Esophagus	27	18	33
Stomach	18	28	46
Colorectum	44	26	25
Pancreas	15	14	61
Larynx	62	26	8
Lung	17	22	48
Breast	48	41	9
Uterus	63	23	12
Ovary	25	6	64
Prostate	61	13	21
Kidney	45	20	30
Bladder	82	9	6
Melanoma	73	12	11
Brain	88	9	1
Thyroid	54	30	14

TABLE 4

AGE AND CANCER RISK	
Incidence in all sites per 100,000	
< 15 years	12
15-24 years	36
25-34 years	119
35-44 years	201
45-54 years	408
55-64 years	790
65-74 years	1,344

different tumors. Note that early diagnosis (local stage) is very much related to organ site and subsequently symptomatology. We must seek those asymptomatic cancers which can be detected and which, if detected early enough, will yield substantially improved survival or cure rates. In this country we do not detect early stomach cancers. This is not because they are undetectable. While they hide from the simple UGI x-ray examination, they are easily revealed by sophisticated procedures like endoscopy and brush cytology. The incidence of stomach cancer in this country is much too low to justify using even simple UGI x-ray examinations on symptomless populations. In Japan, where stomach cancers are relatively common, routine endoscopy and gastric cytology "pay off." There, early and sophisticated detection techniques do result in survival differences.

Even if common in this country, some cancers are rarely found early enough. Thus lung cancer, the leading cancer in men in this country, is NOT WORTH screening for blindly!! Here the problem is not incidence but the lack of effective screening procedures. Unfortunately, the chest x-ray, when positive, is usually too late a sign. Systemic spread has already occurred in the majority of cases. In a recent study of a large group of high risk smokers, screening with sputum cytology and chest films done

TABLE 5

CANCER INCIDENCE BY SEX	
<i>Female</i>	
Breast	20/100,000
Colon Rectum	15/100,000
Lung	12/100,000
Uterine/Cervix	8/100,000
Ovary	7/100,000
<i>Male</i>	
Lung	52/100,000
Colon Rectum	20/100,000
Prostate	15/100,000
Pancreas	9/100,000
Stomach	8/100,000

three times a year did not improve survival from lung cancer. This prospective study compared survival figures from an equally large smoking group who only had annual testing. There was no difference in survival figures for either group. Until better techniques are found, lung cancer screening, even in the high risk smoking population, does not seem fruitful.

What then should constitute a simple effective realistic cost-effective cancer screening examination for a symptomless population? There have been several innovative attempts to concentrate screening on a few "detectable" cancers. One such example is the CANSCREEN clinic concept. CANSCREEN clinics screen for increased risk factors for a few common female cancers, thus focusing on identifying a smaller at-risk population. They use nurse practitioners instead of the more expensive and sometimes less observant physician. They do *not* incorporate the standard chest roentgenogram, the standard biochemical profiles or the standard proctoscopy, all of which have quite low yields and in the aggregate are quite expensive. Instead they include the inexpensive Pap smear, stool guaiac, urinalysis, hemoglobin and a physical examination of the skin, oropharynx and breasts. The average cost of cancer detection screening was about \$36 per patient studied in 1975. The average cost of finding a single cancer was \$5,400. By contrast, in that same year the average cost of the standard physician exam and tests was \$105, with the average cost of finding a new cancer about \$16,000. Abbreviated nurse examinations which focus on common or easily diagnosed cancers in higher risk patients are cheaper and cost-effective.

There are several variations of the simple cancer screening idea. One is for the practicing physician to review each of his/her patients for cancer risk factors, to teach breast self-examinations and to encourage female patients in its monthly practice. The oropharynx is a much neglected site of easily detectable and curable cancer. So also are the skin, the cervix, the testes, the prostate and the rectum. A simple examination on persons of the appropriate sex and age should include, e.g., inspection of the skin and oropharynx, a testicular and rectal examination with stool guaiac. This procedure would neither be exhor-

bitant nor time consuming. More specific tests can be reserved for specialized risk-factor groups or for patients with symptoms. Table 4 presents an example of the influence of the simplest risk factor—*AGE*—on the incidence of cancer. Table 5 reminds us of the important sex related cancers by incidence. Using this information, the imperative of investigating suspicious symptoms in a 65 year old woman becomes obvious. So does the imperative of doing a simple cancer screening examination on a *symptomless* 65 year old woman. To summarize, even in the absence of symptoms or specific high risk factors, where age and sex are the only indications, a simple, low cost, rapid, effective cancer screen can be done. CANCER of the SKIN, BREAST, PROSTATE/TESTES, COLORECTUM, CERVIX, BLADDER and OROPHARYNX can be effectively screened (see Tables 6 and 7). Streamlining these examinations to account for age, sex, smoking and other risk factors may be ultimately as effective in curable cancer detection. Aspects of this simple cancer screening are discussed below.

Least controversial in an annual cancer screening examination is the breast exam. In a recent study by the Health Insurance Plan of New York, mortality from breast cancer was reduced among screenees by 30%. The screen included breast examinations and mammography. The latter screening technique has been the subject of concern because the radiation exposure involved (though small) is potentially hazardous when accumulated over the years. As it happens, mammography is less useful in younger women and of course they are at less risk of having breast cancer at the earlier ages. Currently the National Cancer Institute recommends that routine mammography for symptomless women should be reserved for women over 50 years of age. Monthly Breast Self Exam makes sense at any age. Teaching it should be a routine part of the "exam."

Pap testing has been used extensively since the 1940's. Yet there is evidence to suggest that the incidence of carcinoma of the cervix was decreasing before Pap testing could possibly have been instrumental either in decreasing incidence of invasive carcinoma or in improving survival. Perhaps better hygiene or the high rate of hysterectomies has resulted in the decreasing incidence. Still the Pap smear is credited with the early detection of cervical carcinoma in situ. In turn such detection must influence mortality rates from cervical cancers. Currently a higher rate of detection can be expected among those of low income, those who had early first coitus, and/or many partners (particularly if uncircumcised). Some would exclude its routine use in low risk women (e.g., the celibate female).

The skin examination is simple. Carcinomas of squamous cell and basal cell types are eminently visible and curable. Screening for malignant melanoma is more difficult to justify. Small lesions may be quite lethal and it is therefore unclear that annual skin screening would alter survival.

Colorectal carcinomas are the second most com-

mon cancers in men and in women in the United States. Positive stool guaiacs are unfortunately all too frequently associated with non-cancerous conditions (80-90%). Nonetheless, 3 specimens collected after a high-bulk, non-meat diet will reduce false-positives considerably. Digital exam can approach 30% of the vulnerable rectal area and is associated with far fewer false-positives. It is however a less acceptable procedure than stool testing. Yearly proctoscopies and barium enemas in asymptomatic people over 40 years of age are simply not acceptable to most patients or their doctors. The procedures are too time consuming, uncomfortable, costly and worst of all they have low yield. As an initial screen, stool guaiacs and rectal exam are preferred. A hemoglobin determination should also be obtained. Iron deficiency anemia should instigate further work-up of the gastrointestinal tract for the possibility of cancer.

Testicular exam is easy. Though testicular cancer is rare, it occurs in younger men. It would be unfortunate to miss a testicular mass, since the cure rate is high. Recently, the salvage rate for more advanced lesions has greatly improved. This should be reflected in increased interest in examining for testicular cancers.

Prostatic examination usually underestimates the extent to which the abnormal lesion involves the prostate gland. While there is controversy regarding correct treatment of the early prostatic nodules, biopsy and determination of their histological grade would seem a prudent beginning. Certainly prognosis and the potential of curative treatment depend on making the diagnosis as early as possible.

Urinalysis is simple. As a detection procedure it has limited value except for bladder cancers which are not common. Hematuria however is an early sign of bladder cancer though a late one of hypernephroma. As it is a very simple and inexpensive test, urinalysis would seem a reasonable part of the routine cancer exam.

Examination of the oropharynx is easy and accessible. One might argue that it need not be part of the cancer screen of a symptomless younger person who is a non-smoker and non-drinker. In any case, it is an easy, cheap, and quickly executed examination.

To recapitulate, Tables 6 and 7 highlight simple cancer screening examination for symptomless people.

II. THE HIGH RISK PATIENT

In addition to the simple screen outlined in the previous section, the practitioner would do well to assess each patient for special vulnerability. More sophisticated procedures, more frequent examinations or increased suspiciousness might then be an appropriate response to a particular symptom for one patient but not for another. The following sections review categories of special high risk patients/families of which one should be aware.

A. HEREDITARY SYNDROMES

Several hereditary cancers are known to have a

TABLE 6

SIMPLE CANCER SCREENING IN SYMPTOMLESS WOMEN
Breast Exam
Teach Breast Self-Exam
Mammography (Annual) If Over 50 Years
Pap Smear
Skin Exam
Stool Guaiac and Rectal Exam
Oropharynx Exam
Hemoglobin
Urinalysis

TABLE 7

SIMPLE CANCER SCREENING IN SYMPTOMLESS MEN
Testicular Exam
Prostate Exam
Stool Guaiac and Rectal Exam
Skin Exam
Oropharynx Exam
Hemoglobin
Urinalysis

clear genetic etiology. These patients have family members at high risk for developing special cancers. These include familial polyposis coli. This condition, though occurring in about 1 in 8000 people, provides the practitioner with an excellent chance to control cancer. Recognition of multiple colonic polyps in a high risk patient should be followed by prophylactic colectomy. Such action will prevent colonic cancer in these very vulnerable patients. Without surgical intervention, 100% of the patients will develop a colonic carcinoma by age 50. Polyposis coli is an autosomal dominant disorder. All family members should be screened.

Hereditary multiple endocrine adenomatosis syndromes (MEA) have an autosomal dominant inheritance pattern as well. There are three main types:

Type I: Wermer's Syndrome: Tumors of the pituitary, (usually nonfunctional), parathyroid, and pancreatic islet cells (insulinoma, Zollinger-Ellison Syndrome, gastrinoma). Recognition of family members with subclinical disease is useful. Patients with Zollinger-Ellison Syndrome or insulinoma should be screened for hyperparathyroidism and vice versa.

Type II: Sipple's Syndrome: Tumors include pheochromocytomas (bilateral), medullary carcinoma of the thyroid and parathyroid tumors.

Type III: Medullary carcinoma of the thyroid, pheochromocytomas, parathyroid tumors and multiple mucosal neuromata and intestinal ganglioneuromata.

Identification of a proband can be of great benefit in monitoring MEA II and III family members for the

TABLE 8

HEREDITARY SYNDROMES (Autosomal dominant)	
Polyposis Col I	Polyps degenerate to colonic cancer in 100% patients by age 50.
MEA I	Association of adenomas of the pituitary, parathyroid and pancreas.
MEA II	Association of pheochromocytoma, medullary carcinoma of the thyroid, and parathyroid adenomas.
MEA III	Association of pheochromocytoma, medullary carcinoma of the thyroid, parathyroid adenomas and multiple mucosal neuromas and intestinal ganglioneuromata.
Gardiner's Syndrome	Colonic polyps degenerate into cancer. Osteomas develop. Occasional thyroid and adrenal neoplasms develop.

development of tumor. Increased calcitonin levels have proved to be accurately predictive of small and even microscopic medullary carcinomas of the thyroid. Prophylactic thyroidectomies have been curative (see Table 8).

B. PRE-NEOPLASTIC SYNDROMES

Some autosomal dominant non-malignant syndromes may be associated with an increased risk for developing cancer. An example is neurofibromatosis, an autosomal dominant disease occurring in 1 to 3000 live births. There is an increased risk of developing visceral sarcomas, acoustic neuromas, pheochromocytomas and brain tumors (see Table 9). Recognition of these rare syndromes can help the physician considerably in recognizing the importance of various unusual signs. For example, a patient or family members with neurofibromatosis may have minimal peripheral evidence of the disease—perhaps 1 or 2 café-au-lait spots and yet have an increased incidence of brain tumors. In one reported family of 97 members, 55 had acoustic neuromas!

C. GENETIC DERMATOSES

These are mainly autosomal recessive diseases and are quite rare. Recognition of the condition in a patient can increase the physician's level of suspicion of a particular symptom because of the associated development of specific cancers (see Table 10).

D. PARANEOPLASTIC DISEASES

I. NON-CANCEROUS DISEASES ASSOCIATED WITH CANCERS

In this group of diseases, genetic factors may or may not play a role in the development of associated cancers. To date, no specific gene defects have been linked with the development of cancers. Nonetheless, patients who have the following diseases are at risk for the development of the listed cancers. The mechanisms are really unknown.

Disease	Cancer Incidence Increased
Scleroderma	Bronchiolar Carcinoma
Dermatomyositis	Adenocarcinoma of Viscera

Sjogren's	Lymphoma
Systemic Lupus Erythematosus	Thymic Tumor Lymphoma Leukemia
Down's Syndrome	Leukemia
Paget's Disease	Leukemia Osteogenic Sarcoma
Ulcerative Colitis	Colonic Carcinoma after 20 yrs: 25% cancer after 30 yrs: 40% cancer
Cirrhosis of Liver	Hepatoma
Colonic Polyps	Colonic Carcinoma
Pernicious Anemia	Gastric Carcinoma
Achlorhydria	Choriocarcinoma
Molar Pregnancy	30x ↑ Testicular Carcinoma Even when there is early surgery. Either testis at risk.
Undescended Testes	

II. CANCERS ASSOCIATED WITH OTHER CANCERS

Patients cured of one cancer may be at greater risk for the development of other cancers. The reason for the association is unclear, although multi-organ exposure to similar carcinogens may be one mechanism. As cancer therapy improves we should begin to see more of these second associated cancers:

"Cured"	Associated New Cancer
Breast	Other Breast 1% per year Colon Cancer 5% Uterine Cancer 1.5x ↑ Ovarian Cancer 1.5x ↑
Uterus	Rectal Cancer 1.5x ↑
Cervix	Rectal Cancer 1.5x ↑
Nasal Cavity or Skin or Nasopharynx	Skin Cancer 20% or UGI Cancer 73%
Oral Cavity	Oral Cavity: 40% new or recurrence if continues to smoke
Colon	Colon Cancer 5x ↑ Prostate Cancer 4x ↑ Ovarian Cancer 7x ↑
Hodgkin's Disease	Leukemia 35x ↑ especially if heavily treated with chemo- and radiotherapy
Ovary	1% Leukemia if treated with alkylating chemotherapy

E. FAMILIAL CANCERS

There are families which develop a high incidence of certain tumors without obvious genetic patterns. These families are rare and usually have cancer of the colon or uterus affecting family members at progressively earlier ages with each succeeding generation. In addition, familial cancers are classically multiple in site, whereas non-familial cancers tend to be unifocal. It is unclear whether the risk that family members have is genetically determined or environmentally influenced or a combination thereof. What is important is that these rare families must be recognized and screened appropriately.

In addition to cancer-families, any first degree relative will have increased risks for certain cancers.

TABLE 9

PRENEOPLASTIC SYNDROMES (Autosomal Dominant)		
Sign/Symptom	Syndrome	Associated Tumors
Cutaneous	Neurofibromatosis	Visceral sarcomas
Endocrine		Acoustic neuromas
Ocular lesions		Brain Tumors
Skeletal		(5-20% get some tumor)
Visceral		
Adenoma sebaceum	Tuberous Sclerosis	
Epilepsy		
Mental Retardation	von Hippel-Landau	3% Intracranial Neoplasm
Angiomatosis of Retina and Cerebellum		Hemangioblastoma of cerebellum
		Hypernephroma
Hamartomas	Peutz-Jegher's	Pheochromocytoma
G.I. Polyps		Rarely adenocarcinoma of colon, duodenum
Melanin Spots		5% women ovarian cancer
Osteo-chondromas	Multiple Exostoses	5-10% chondrosarcoma

TABLE 10

GENETIC DERMATOSES (Autosomal Recessive)	
Associated Cancers	
Ataxia Telangiectasia	GI cancers, especially gastric; Leukemia, Lymphoma
Xeroderma Pigmentosum	Basal cell carcinoma Squamous cell carcinoma Malignant melanoma
Albinism	Basal cell carcinoma Squamous cell carcinoma
Werner's (Progeria)	Sarcoma Meningioma

The increased risk for the family member is usually about three times that of the general population. Unlike the true familial cancers, there is no tendency to develop multiple cancers at earlier ages.

If family member (first degree) has: breast, prostate, uterus, lung, stomach, colon carcinoma or melanoma then patient has 3x ↑ increased risk of developing the same cancer.

Breast cancer, so common in the United States, is clearly influenced by family history. It is probably also heavily influenced by such things as hormones, diet, weight and parity. A careful family history can define the extent of risk more precisely (see Table 11). The increased risks clearly suggest a more powerful familial (? genetic) influence for premenopausally developing breast cancer.

F. MISCELLANEOUS CONDITIONS

Special consideration should be given to our mobile society. There are cultural and geographic

TABLE 11

BREAST CANCER RISKS	
<i>If First Degree Female Relative Had Breast Cancer...</i>	<i>Patient Has Risk Of Breast Cancer</i>
	<i>Increased</i>
When pre-menopausal, with unilateral breast involvement	3x
When pre-menopausal, with bilateral breast involvement	9x
When post-menopausal, with unilateral breast involvement	1.5x
When post-menopausal, with bilateral breast involvement	3x

TABLE 12

MISCELLANEOUS ASSOCIATIONS WITH INCREASED CANCERS	
Cantonese Chinese	Nasopharyngeal Cancer (independent of their geographic location, generation)
Japanese	Gastric Cancer (high as first generation; lower as they are acculturated)
Finns	Gastric Cancer
Icelanders	(probably related to salted diet)
Africans	Hepatoma (due to aflatoxins)
Rhodesians	Bladder Cancer
Mozambiqueans	(due to schistosome parasite)
Egyptians	
Japanese	Hepatoma
Koreans	(due to <i>Clonorchis sinensis</i>)
Chinese	
Taiwanese	
Indochinese	
Higher socioeconomic groups	Breast Cancer
	Uterine Cancer
Lower socioeconomic groups	Cervical Cancer
	Lung Cancer
Non-Circumcised Penis	Cancer of Cervix (in partner)
Phimosis	Penile Cancer

flavors to the cancer incidence charts. People who have been exposed to specific environments and/or who have certain racial, socio-economic affinities may be at greater risk for certain tumors. We are not clear what the etiologic factors are, but it is well to recognize the special vulnerability of a particular patient (see Table 12).

III. HIGH RISK PATIENTS: CARCINOGEN EXPOSURE

Carcinogen exposure is probably the most important area in which the practicing physician should become involved. If there is a dim prospect of finding cancers early enough to treat, then possibly we should examine the areas where we might prevent cancer from occurring or at least decrease exposure to known carcinogens. Practitioners of adult

Continued on Page 285

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATIONS: For the prevention and treatment of nocturnal recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis, and static foot deformities.

CONTRAINDICATIONS: Because of the quinine content, Quinamm is contraindicated in women of childbearing potential, in pregnancy, in patients with known quinine sensitivity, and in patients with glucose-6-phosphate dehydrogenase deficiency. Hemolysis (with the potential for hemolytic anemia) has been associated with a G-6-PD deficiency in patients taking quinine.

PRECAUTIONS: Thrombocytopenic purpura may follow the administration of quinine in highly sensitive patients. Recovery will follow withdrawal of the medication. Cinchona alkaloids, including quinine, have the potential to depress the hepatic enzyme system that synthesizes the vitamin K-dependent factors. The resulting hypoprothrombinemic effect may enhance the action of warfarin and other oral anticoagulants.

ADVERSE REACTIONS: Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. If ringing in the ears, deafness, skin rash, or visual disturbances occur, the drug should be discontinued.

DOSAGE AND ADMINISTRATION:

1 tablet upon retiring. When necessary, 1 additional tablet may be taken following the evening meal.

Product Information as of September, 1977
U.S. Patent 2,985,558

Merrell

MERRELL-NATIONAL LABORATORIES Inc
Cayey, Puerto Rico 00633

Direct Medical Inquiries to:
MERRELL-NATIONAL LABORATORIES
Division of Richardson-Merrell Inc.
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TABLE 13

**CIGARETTE CONSUMPTION
AND THE RISK OF DEVELOPING LUNG CANCER**

1 pack per day for 15 years = 109,500 cigarettes, or 15 pack years.

The risk of developing lung cancer is 1% or 1/100 of a similarly exposed group.

<i>If Patient Has</i>	<i>Risk Now</i>	
60 pack years	1 of 20 similarly exposed smokers or	5%
90 pack years	1 of 12 similarly exposed smokers or	8%
100 pack years	1 of 8 similarly exposed smokers or	13%
120 pack years	1 of 5 similarly exposed smokers or	20%
> 135 pack years	1 of 3 similarly exposed smokers or	33%

medicine in this country have been unenthusiastic about prevention for far too long. Many doctors believe cure is *the* only goal in medicine and that early diagnosis the only imperative. But there are other goals. In this case, preventing disease can be thought of as a *pre*-diagnostic imperative. For many, prevention seems an unexciting task but it is the activity most likely to improve world health.

For many doctors, crisis medicine with its inherent excitement and dramatic outcomes is much more appealing. By contrast, talking publicly and privately about the known causes of cancer seems less important. Yet cancer-causing agents are quite well known. Many have been known for years, even decades. There is hard evidence indicting 20 carcinogenic substances about which we physicians should be quite clear. Consequently, we should include a careful and complete carcinogen exposure in our history taking: how much, how long, when.

Lung cancer, is the leading cancer of American men, and its rate is rising alarmingly among women. If we want to make a genuine improvement in the cure rates for lung cancer, there is currently only one sure way to do it. Early enough diagnosis at least today is impractical and impossible. The only imperative one can have with regard to curing lung cancer is to get our patients to stop smoking. If we can do this we will "cure" 22% of all male cancers! We could cure 66,000 men and 21,000 women a year or prevent about 25% of all cancer deaths. Most physicians will never see a case or treat a family member of polyposis coli, but lung cancer and all the respiratory problems of smoking are a frightening reality. At least 25% of all American cancers are due to tobacco use. Thus is *the pre*-diagnostic imperative in cancer medicine.

What if anything can be done to improve early diagnosis among tobacco users and that subgroup of smokers who also have *co*-carcinogenic exposure? Table 13 outlines some important associations between length and amount of cigarette smoking and the risk of lung cancer development.

Consider this: a 65-year-old-man smoking 2 packs per day since teenage would have a 20% chance of developing lung cancer, in addition to the increased risk of developing other cardio-respiratory diseases and carcinogen-related cancers. Of all the carcinogen exposed population, none is so numerous as tobacco

TABLE 14

Tobacco Users

Increased Risk Of

Pancreas Cancer 3x†
Bladder Cancer
Renal Cell Cancer

Tobacco Users Plus

Radioactive mining exposure 10-20x† Respiratory Cancer
Asbestos exposure 10-20x† Respiratory Cancer
Heavy alcohol ingestion Esophageal Cancer
Oropharynx Cancer

users, especially cigarette smokers. Table 14 lists the other cancers for which tobacco users are at high risk.

When taking a history from any patient, be sure to ask:

Does she/he smoke?

How many cigarettes a day for how many years?

Did she/he smoke unfiltered/filtered cigarettes?

Has there been a change in her/his smoking habits?

Is there pipe, cigar, chewing tobacco use?

ask about *co*-carcinogens, too:

Has there been asbestos exposure—ever? How long? What job?

Does he/she drink alcohol? How much? How often? How long?

Has he/she ever worked in mines? Which ones? How long?

Has he/she worked in petroleum industries? Which? How long?

Co-carcinogenic exposures are frighteningly additive, particularly in terms of increasing the risk of developing lung cancer. If a patient has worked with or been exposed to asbestos (there are millions of exposed shipyard workers and other people), *and* that patient is also a smoker, then the calculated risk for developing lung cancer is 20 times the risk of a non-exposed smoker! Equally serious *co*-carcinogens include mining exposures to tungsten, iron, lead, nickel, arsenic, cobalt, bismuth or uranium. A person smoking over 20 cigarettes a day with a heavy uranium mining exposure has a 13 times greater increase in the risk of respiratory cancer deaths than a similar smoker with no mining exposure or a non-smoking miner. Will added vigilance on the part of the family practitioner result in earlier diagnosis and subsequently improved survival figures? One certainly hopes so, but there is no hard evidence to prove this point. That is why prevention of lung cancer by decreasing carcinogen exposure is so important.

There are other important and even common carcinogens. The cancers associated with these carcinogens are listed in Tables 15 and 16. Cancer histories should include queries regarding exposure to these materials, the length of, amount of and timing of that exposure. Appropriate screening should be instituted in patients at risk.

IV. HIGH RISK PATIENTS: SPECIAL CANCERS AND THEIR RISK FACTORS

Sometimes it is useful to look at a list of cancers

TABLE 15

CARCINOGENS AND CANCER RISK	
<i>Chemicals: Organic</i>	<i>Risk of Cancer</i>
Soot	Scrotal Skin
Coal Tars: Lignite	Skin
Bituminous	
Anthracite	
Coal Tars: Fumes	Lung
Creosote Oil	Skin
Anthracene Oil	(usually hands, face, neck)
Paraffin Oil (Shale Oil)	
Petroleum Oil	
Petroleum Lubricating Oil	
Shale Lubricating Oil	
Aromatic Amines	Bladder, Ureter, Kidney
(Dye intermediates)	
Isopropyl Oil	Nasal Passages, Sinuses, Larynx, Lung
Mustard Gas	Lung
<i>Chemicals: Inorganic</i>	
Arsenic	Skin
Asbestos	Lung
Chromates	Lung
Nickel	Lung, Nasal Cavity, Sinuses
<i>Physical Agents</i>	
Ultra Violet Light	Skin
X-Irradiation	Skin, Leukemia
Radioactive Substances	Lung, Skin, Leukemia, Bone

and their special risk factors rather than as we have been doing, looking at the exposure history or family history. If one has any suspicion that bladder cancer might be a possibility in a patient with microscopic hematuria, knowing the special factors which increase that possibility may be helpful in deciding whether or not to undertake an exhaustive or a simple workup. Knowing that the patient smoked, worked with dyes and had cyclophosphamide chemotherapy for a lymphoma treated 10 years ago should underscore the imperative for diagnosing the cause of hematuria and especially for ruling bladder cancer in or out.

Table 17 lists symptoms which if associated with certain carcinogens, positive family histories, or other conditions, should arouse the physician's suspicion that a particular cancer may be the cause of that symptom or sign.

V. SIGNS AND SYMPTOMS

As mentioned earlier, signs and symptoms caused by cancers are unfortunately often indicative of advanced disease. But not always. Sometimes they herald curable stages. No chart or table can outline the most important of all ingredients in the diagnostic imperatives for cancer: clinical judgement. If we wait too long to diagnose, what chances do we have with the already low cure rates? Are there some signs and symptoms which are more likely to yield better (or worse) cure rates? Are there important enough differences between cure and palliation to warrant increased diagnostic procedures? If we wait,

TABLE 16

IATROGENIC CARCINOGENS AND CANCER RISKS	
<i>Iatrogenic Carcinogens:</i>	
<i>Hormones</i>	
DES (Diethylstilbesterol)	Vaginal Cancer
Estrogen Replacement (postmenopausal pt)	Uterine Cancer, ? Breast Cancer
Birth Control Pills (premenopausal pt)	Liver Cancer, ? Breast Cancer
Androgens	Liver Cancer
<i>Iatrogenic Carcinogens:</i>	
<i>Cytotoxic Agents</i>	
Alkylating Agents (Chlorambucil, Cyclophosphamide, Nitrogen Mustard, L- Phenylalanine)	Leukemia
Cyclophosphamide	Bladder Cancer
<i>Iatrogenic Carcinogens:</i>	
<i>Ionizing Radiation</i>	
Radiotherapy	Cancer of the irradiated organ
¹³¹ I	Leukemia
³² P	Leukemia
Thorotrast	Leukemia
<i>Iatrogenic Immunosuppressants</i>	
? "Carcinostimulants"	10% get Cancers
? "Carcino-permitters"	Especially Skin
(esp. renal transplant patients)	Lymphoproliferative Disorders

will the quality of life be seriously flawed? These questions are, in the long run, the most difficult and the loneliest. In the case where saving a life is improbable and increasing survival time unlikely, what difference does it make if we make the decision to diagnose now or later? How imperative is the decision to diagnose the unhelpable, untreatable, incurable? Agonizing over the proper timing of diagnosis is a unique dilemma. Should one push ahead for the immediate diagnosis of advanced cancer of the pancreas or wait until making the diagnosis is irrelevant? Making the diagnosis sooner rather than later may rob the patient and the family of innocent moments. Or it may prevent them from acknowledging their concern for each other and delay the inevitable bittersweet process of honest sharing. The imperatives are moral as much as medical or scientific. No formula is at hand to ease the doctor's conscience. My own imperative is that honesty remains the best policy. Because patients deserve to know and to have the opportunity to formulate their own decisions, not pursuing the diagnosis (even when it may be "obvious") robs them of their right to know what is. Delay therefore means that they will be sicker when they do find out the truth. Then they will be less able to deal with their fears, their pain, and all the other inevitable issues which arise. Cancer presents the physician, particularly the family physician, with complicated decisions. The moral and the medical are inextricably entwined.

TABLE 17

<i>Sign/Symptom</i>	<i>plus Risk Factors</i>	<i>Be Sure To Rule Out Cancer of</i>
Hematuria	Tobacco Tars (smokers) Cyclophosphamide treated patients Rubber, cable, leather and paint workers Aromatic amine workers (intermediate dyes) Bilharziasis exposed patients (Egypt) ? Coffee drinkers	Bladder
Breast Lump	1st degree relative with + family history (see Table 11) esp. premenopausal relative with bilateral breast cancer: 9x ↑ Fibrocystic breast disease 2x ↑ Early menarche, late menopause 3x ↑ Late first parity (after 40) 3x ↑ Some hormone users 3x ↑ Prior low dose radiotherapy fluoroscopy 3x ↑ Prior breast, uterine, colon or ovarian cancer 1.5x ↑	Breast
Bone Pain/Lump	Paget's Prior radiotherapy, radiation exposure	Bone
Positive Stool Guaiac, or Polyps, or Iron Deficiency Anemia, or Abnormal Rectal Exam	Prior colon cancer Ulcerative colitis Crohn's Prior uterine cancer 1.5x ↑ Prior cervical cancer 1.5x ↑ Familial polyposis coli Cancer family 1st degree relative with colonic cancer 3x ↑ Gardner's Peutz Jegher's	Colon Rectum
Dysphagia	Smoker and drinker Plummer Vinson (sideropenia) Lye strictures Esophageal Leukoplakia	Esophagus
Right Upper Quadrant Pain	Aflatoxins (moldy peanut eaters)	Liver

VI. SIGNS AND SYMPTOMS: THE 7 WARNING SIGNS

The American Cancer Society has urged every person and every physician to pay special heed to these 7 Warning Signs of Cancer. How many really warn of early curable cancer?

THE 7 WARNING SIGNS OF CANCER

1. Change in bowel or bladder habit.
2. Sore that does not heal.
3. Unusual bleeding or discharge.
4. Thickening or lump in breast or elsewhere.
5. Indigestion or difficulty in swallowing.
6. Recent change in mole or wart.
7. Cough or hoarseness.

1. A change in bowel habits: This symptom is quite elusive. Most of us are not so perfectly or rigidly regular that some change is not a part of our normal pattern. If we insist that the change from normal be important, e.g., of long duration, perhaps of several months or a decrease in size to pencil caliber, then we will find less curable disease. Significant and persistent change of bowel habit is generally a late sign. Nonetheless, investigation with rectal exam, stool quaiac, proctoscopy, barium enema, and if necessary, colonoscopy, is in order. The yield of curable cancer will be low.

2. Sores that do not heal: Usually these lesions are skin cancers, basal cell or squamous cell. Although their growth is slow, one should try to make the diagnosis early, because squamous cell carcinomas of the skin may metastasize. Oral ulcers can be early presentations of oral pharyngeal cancers, and should never be overlooked.

3. Unusual bleeding or discharge: Blood in the stool is a late sign of bowel cancer. Hemoptysis is a late sign of cancer of the lung. By contrast, vaginal bleeding is an early sign of uterine cancer or cervical cancer and should never be overlooked. Nipple bleeding or discharge, as a sign of breast cancer, may be compatible with an excellent salvage rate. *Spontaneous* or bloody nipple discharge should never be ignored. Mammography with aspiration of the nipple and cytologic examination of the fluid may make the diagnosis. Otherwise subareolar excision should be undertaken to exclude the diagnosis of curable cancer.

4. Lump in the breast (or elsewhere): In most sites, palpable masses are late signs of cancer, e.g., lymph node metastases. But in the breast, a lump frequently indicates resectable and curable tumor. In a postmenopausal woman, a discrete breast lump should be regarded as cancer until proven otherwise. New thickenings should also be biopsied. Aspiration of

TABLE 18

DIAGNOSTIC IMPERATIVE: PAIN	
<i>Pain Location</i>	<i>Cancer Which May Be Curable</i>
Muscle	Sarcoma
Bone	Primary Bone Neoplasm (not metastases)
Scrotum	Testicular Cancer
Prevoiding Pain	Bladder Cancer
Arm/Shoulder/ Scapula/Upper Anterior Chest	Pancoast Tumor of the Lung (10% are curable with radiotherapy and surgery)
Mouth	Oropharyngeal Cancer
	<i>Infrequently Associated with Curable Cancer</i>
Flank Pain	Renal Cell Cancer
Right Upper Quadrant Pain	Hepatoma
Dysphagia	Esophageal Cancer

TABLE 19

DIAGNOSTIC IMPERATIVE: BLEEDING	
<i>Site</i>	<i>Curable Cancers (Early Symptom)</i>
Nipple	Breast Cancer
Hematuria	Bladder Cancer
Bright red blood per rectum	Rectal Cancer
Vaginal	Cervical or Uterine Cancer
Melena	Colorectal Cancer (Intermediate Symptom)
	<i>Rarely Curable Cancers (Late Symptoms)</i>
Hemoptysis	Lung Cancer
Hematemesis	Stomach Cancer
Hematuria	Renal Cell Cancer

cyst fluid, or needle biopsy of solid lumps can be done in the office under local anesthetic. Biopsy should be done as a separate procedure from the definitive surgery if such is contemplated. In premenopausal women, one can safely watch a lump for a menstrual cycle or two. If the lump is not regressing or gone, biopsy is needed. General lumpiness (fibrocystic disease) is a very difficult matter to be sure about. The combination of the patient's own expertise [monthly breast self examinations], the doctor's examination, and mammography \pm thermography may be sufficient if there is no discrete mass. If there is ANY suspicion of cancer, biopsy must be done.

5. Difficulty in swallowing and indigestion: These are late symptoms of esophageal and stomach cancers.

6. Change in a wart or mole: If malignant melanoma is diagnosed promptly, the chance that spread has not occurred varies from 50-95% depending on the depth of skin invasion. Never burn off any lesion which could remotely be melanoma. The proper diagnosis is made by excisional biopsy. Prompt diagnosis will make a difference. How great a difference will depend on the biologic nature of the melanoma.

TABLE 20

DIAGNOSTIC IMPERATIVE: LUMPS (MASSES)	
<i>Site</i>	<i>Frequently Curable Cancers</i>
Breast	The Important Lesion: < 2 cm lesion with negative lymph nodes (Stage I) has 90% + 5 year survival. This should never be missed. Stage II Lesion: (2-5 cm lesion without positive lymph nodes have 50% 5 year survival). Still a curable lesion. When In Doubt, Biopsy. Cure rate has improved from 44% (1950) to 66% (1970). Earlier diagnosis has played a vital role.
Thyroid	Nodules: solitary or cold on scan: 17% cancer. Multinodular Goiter: < 5% had cancer.
Cervical Lymph Nodes	Even if Hodgkin's or Thyroid Cancer, 90% curable or long term survival. Salivary Gland Cancer Paraganglioma (over carotid body)
Mediastinum	Hodgkin's Thymoma (without symptoms, 60% alive at 5 years). Germ Cell Cancers (50% alive at 10 yrs with therapy).
Subcutaneous in Muscle, Periosteum	Sarcoma
Testes (including change in hydrocoele)	Testicular Carcinoma
Prostate	50% will be Cancer, of which 1/4 will extend beyond gland. Biopsy will influence treatment decision. If cancer is well-differentiated: expectant therapy vs. surgery vs. radiotherapy if anaplastic, aggressive surgery and/or radiotherapy.

7. Cough and hoarseness: Unfortunately persistent cough and hoarseness are very late symptoms of lung cancer and almost never lead to diagnosis of curable cases. However, they may be symptoms of early laryngeal cancer, and they should therefore be promptly investigated for this possibility.

In summary, the 7 well known signs of cancer are not necessarily the harbingers of curable disease.

VII. LOCAL SIGNS AND SYMPTOMS: IMPORTANT ONES NOT TO MISS

A. *Pain*: While pain is often a late sign and signifies invasion of sensitive tissues, particularly bone, still pain should be considered a symptom of curable or at least treatable disease, until proven otherwise (see Table 18).

B. *Bleeding*: This may be an early sign of some cancers, though a late one for other cancers. Table 19 presents the relative imperatives. Causes of bleeding which might represent early cancers should not be missed.

C. *Lumps (masses)*: Lumps should be biopsied so that the appropriate diagnosis can be made. Table 20 lists 10 organ sites where the presenting lumps or masses represent tumors which have a reasonable chance for cure. They should therefore not be

TABLE 21

DIAGNOSTIC IMPERATIVE: ULCER/SORE

<i>Site of Curable Cancers if Delay is Minimal</i>	
Eyelid	Easily visible, chronic ulceration on the eyelid could be a basal cell carcinoma. Early therapy is curative and prevents insidious encroachment on nearby structures, such as the eye. The eye will have to be sacrificed otherwise.
Oropharynx	A highly curable site if the tumor is seen early (75% cure rate for early localized lesions). Plaques red/white should always make the physician suspicious. Biopsy is indicated. The tongue and floor of the mouth yield 75-90% cure rates, if diagnosed in the early localized phase. Biopsy any persistent (>14 day old) ulcer, even if asymptomatic and particularly if erythroplastic.
Skin	Basal Cell Carcinomas: These are slow growing. Sun exposed areas. Rarely metastasize. Can be insidious, locally invasive. Squamous Cell Carcinomas: slowly growing, metastasize, in sun damaged skin, premalignant actinic keratosis should alert.
Breast	Paget's Disease of Nipple: Do very well if there is no underlying tumor. Do very well if diagnosed early.
Gastric Ulcers	Even if healed, one should probably biopsy the seemingly benign ulcer. In 10% of cases, these healed ulcers will conceal a gastric cancer.
Anus	Non-healing ulcer, fistulae should be biopsied.
Cervix	Dysplasia (Pap smear diagnosis) if untreated will develop into cervical carcinoma in 80% of women by 10 years. <i>In situ</i> carcinomas are less well behaved. Do not neglect to do a Pap smear, particularly on the higher risk women: over 40, with many partners, or who had early coitus.
Vagina	In the older woman, leukoplakia are pre-cancerous lesions. Biopsy if persistent.
Penis	If there is an unhealing ulcer, biopsy it.

neglected. When in doubt, biopsy. Different tissues require different techniques for biopsy. For example, suspicious muscle masses should *not* be removed by cutting through fascial planes.

D. *Ulcer/Sore*: Some are not noticed by the patient either because they are hidden or because they do not cause pain or other disturbing symptoms. But these are easily found if the doctor or nurse looks. Any non-healing persistent ulcer should be biopsied. Two weeks is long enough to wait. Table 21 lists common sites for *curable* ulcers: don't miss them.

E. *Neurological symptoms*: These generally indicate non-curable disease, but even so, palliation is an important imperative. Neurologic symptoms and signs often herald imminent disaster. The wary diagnostician will not wait to make diagnostic and therapeutic decisions. Table 22 lists common symptoms which should be attended to promptly, so that intact neurologic functioning can be maximized.

F. *Miscellaneous*: These are symptoms not infre-

TABLE 22

PALLIATION IMPERATIVE: NEUROLOGICAL SIGN

<i>Sign/Symptom</i>	<i>Preserve Maximal Function</i>
Horner's Syndrome ptosis, miosis, anidrosis epiphthalmos	Sympathetic nerve paralyzed in the cervical lymph node chain. Prompt radiotherapy may reverse symptoms.
Upper Extremity Weakness/Pain	Thoracic outlet pancoast tumor. 10% can be cured. Many more can be relieved of needless pain, or loss of function.
Back Pain, Paresthesia, Urinary Retention, Weak- ness, Loss of Bowel Control	Impending spinal cord compression. Usually begins with central pain then parasthesia and lastly bowel dysfunction. Early diagnosis is the difference between permanent loss of function and return of function. Usually occur in known cancer patients.
Confusion/Head- ache/Nausea Vomiting	Increased intracranial pressure. Don't do lumbar puncture. Early Diagnosis may save neurological functioning, whether due to primary or secondary brain tumor.
Nausea/Vomit- ing/Lethargy/ Confusion/Consti- pation/Polyuria	Symptoms of hypercalcemia, a potential fatal electrolyte imbalance. Easily treated. Seen esp. in patients with breast cancer, prostate cancer, myelomas or any cancer widely metastatic to bone: (Renal cell, head and neck, lung cancer).
Focal Lesion/ Stroke/Seizure	Brain tumor a distinct possibility. Whether primary or metastatic, treatment differs and early diagnosis can preserve function.
Personality Change	May be subtle. Think of brain tumor, primary or metastasis.
Carcinomatous Meningitis (Progressive loss of cranial nerve func- tion, neck rigidity, signs of increased in- tracranial pressure)	Most common cause is lymphoma but can be seen in treatable solid tumors like breast cancer. Untreated: all die within 6 weeks. Treated: (radiotherapy/corticosteroids) median survival 20+ weeks.

quently presenting to the physician. They may or may not be early. But regardless, for those patients who present with them, diagnosis should be made promptly to maximize palliation and hopefully to increase survival. Table 23 presents the signs/symptoms.

VIII. SYSTEMIC SIGNS AND SYMPTOMS: COMMONLY RECOGNIZED PARANEO- PLASTIC SIGNS AND SYMPTOMS OF CANCER

Systemic signs and symptoms may be caused by the indirect effects of tumors, usually advanced ones. Some of these remote effects on the body are common. The following four are not only common but synonymous with the lay public's picture of the cancer patient. The mechanisms by which tumors cause these particular constitutional effects are quite complicated and/or unclear.

A. *Anorexia*: This symptom is usually seen in late disease, especially in advanced cancer of the stomach or pancreas. Anorexia may also be a prominent clinical feature if the liver is heavily involved with metastases.

TABLE 23

**DIAGNOSTIC OR PALIATIVE IMPERATIVE:
MISCELLANEOUS SIGNS**

<i>Sign/Symptom</i>	<i>Cancer</i>
Pruritus Vulvae	Vaginal Cancer (early symptom)
Leukoplakia	Oral, Esophageal, Vaginal Sites: All Forewarnings of Cancer (early sign)
Epididymitis	Not subsiding in 2 weeks: Testicular Cancer (curable)
Heart Murmur/ Fever/Syncope/ ESR	Atrial Myxoma (curable)
Iron Deficiency Anemia	GI Cancer Must Be Ruled Out
Bowel Change	Lower Colon (intermediate to late symptom)
Urinary Fre- quency/Nocturia	Bladder Cancer
Tenesmus	Rectal Cancer (late symptom)
Painless Jaundice	Amulla of Vater Cancer. The occasional patient will be operable. Most will benefit from decompression.
Facial Periorbital Edema Increase Venous Pattern, Upper Extremities	Superior Vena Caval Syndrome: see section on Emergency.
Lower Back Pain	The commonest of human complaints. Consider the possibility of metastatic cancer to bone, myeloma early cord compression. Early diagnosis may lead to the relief of needless pain.

B. Weight loss: This is a common accompaniment and "B" symptom of Hodgkin's disease. Though it usually signifies advanced disease, the disease is still compatible with long-term survival (? cure) in over 40% of cases. Weight loss is also commonly seen in cancers of stomach, pancreas and lung. It is almost always synonymous with late-stage disease. It is rarely seen in breast cancer even in advanced states. **NOTE:** It may be seen in early renal cell carcinoma where disease is still confined to the capsule and survival exceeds 50% at 5 years.

C. Fever: This is a common occurrence and "B" symptom of Hodgkin's disease. Fever is compatible with long survivals (? cure) in over 40% of patients with advanced Hodgkin's disease. It is also seen in patients with solid tumor metastatic to liver or bone marrow. Usually the patient tolerates the fever from tumors better than fever resulting from infection. Fever is occasionally an early sign in curable solid tumor. **NOTE:** Fever may be an early symptom of curable renal cell carcinoma.

D. Fatigue: This is a non-specific symptom of tumor and generally a late sign. Though there may be an associated non-specific anemia of chronic disease, it is usually not severe enough to account for the degree of fatigue experienced. Occasionally, fatigue may be caused by iron deficiency anemia. In this case, investigation for gastrointestinal cancers is required. Early carcinoma of the right colon should specifically be excluded.

IX. SYSTEMIC SIGNS AND SYMPTOMS:

OTHER PARANEOPLASTIC SYNDROMES

Paraneoplastic "syndromes" encompass an uncommon group somewhat less frequently observed spectrum of clinical or laboratory abnormalities which are also associated with advanced malignancies. These syndromes do not result from the direct growth of tumor but from the remote or systemic effects of tumor products on various organs. In some instances, the tumor produces a specific hormone or substance which is known to cause or mediate a specific biologic effect. At other times, one merely suspects such a substance has been produced though none is demonstrable. Table 24 summarizes some of the more common "syndromes," the known mediator, and the malignancies which produce these paraneoplastic clinical or laboratory abnormalities (syndrome).

Because most paraneoplastic syndromes occur in the setting of advanced malignancy, their usefulness as diagnostic imperatives is limited. However, some syndromes or markers are associated with tumors which should not be missed. Keep in mind that each of the following tumors may cause more than one syndrome (see Table 24). Aggressive diagnostic procedures should be used when a paraneoplastic "syndrome" suggests any of the following tumors:

OAT CELL CARCINOMAS of the lung are treatable cancers. These days, 50% of patients treated aggressively will live longer than 12 months. Moreover, 50% of patients with localized disease treated aggressively will survive more than 24 months.

PITUITARY, ADRENAL, GONADAL and **PANCREATIC ENDOCRINE** tumors may actually be "benign" but cause very distressing or even lethal effects because of their hormonal secretions. Early diagnosis and surgical extirpation, even if not complete, may immensely improve the quality of life. As small tumors frequently cause severe symptoms, vigorous investigation of these symptoms may lead to complete cure of either benign or malignant endocrine secreting tumors.

MEDULLARY CARCINOMAS OF THE THYROID are eminently curable. If one has a patient with this disease, one should locate family members. If serum calcitonin levels are elevated, medullary carcinoma of the thyroid is present. Elective surgery often results in cure.

RENAL CELL CANCERS may present with a variety of symptoms and still be small and encapsulated. It is therefore worthwhile thinking about them even if they are quite uncommon.

GERM CELL TUMORS are also rare but treatable even in advanced stages. Choriocarcinoma in the female is almost always curable even when advanced. Prompt diagnosis is important in avoiding the sad and fatal consequences of liver or brain metastases. These days the non-seminomatous testicular carcinomas are treatable and have good long term prognoses with aggressive treatment programs.

TABLE 24

<i>Paraneoplastic "Syndrome"</i>	<i>Cause</i>	<i>Tumor</i>
Hyponatremia	ADH	Oat Cell Cancer Lung
Cushings Syndrome	ACTH	Oat Cell Cancer Lung Pancreatic Tumor Pituitary Tumor Adrenocortex Tumor
Hyperpigmentation	MSH	Oat Cell Cancer Lung
Hypoglycemia	MSH	Oat Cell Cancer Lung Pancreatic Tumor
	Glucose ↓	"Sink" Effect 2° Sarcoma Mass or Very Advanced Liver Mets
Lactic Acidemia	Tissue Hypoxia	Acute Leukemia (early) Solid Cancer (late)
Fever/Normocytic Anemia/Leukocytosis	ESR	Renal Cell Cancer (early)
Hypercalcemia	PTH, ? x Factor	Renal Cell Cancer (early)
Abnormal Liver Function		Renal Cell Cancer (early)
Fever or Hematocrit ESR	Erythropoetin	Renal Cell Cancer (early)
	?	Renal Cell Cancer (early)
Weight Loss	?	Renal Cell Cancer (early)
Multiple GI Ulcers	Gastrin	Zollinger Ellison (Pancreatic) Tumor
Pancreatic Cholera (Watery Diarrhea)	VIP	Pancreatic Tumor
Myesthesia-Like Syndrome	?	Lung Cancer, esp. (late)
Acromegaly	GH	Pituitary Tumor
Paroxysmal Hypertension	Catecholamines	Pheochromocytoma

They should not be missed. Needless to say, the earlier the diagnosis, the greater the cure rate.

X. SIGNS AND SYMPTOMS: ONCOLOGIC EMERGENCIES

The disorders considered here are not often subject to cure, but point to life threatening or very serious problems which can be relieved temporarily. Generally they arise in the setting of incurable disease, in patients already known to have advanced cancer. The impulse to treat should be tempered with the knowledge of the patient's life situation. Correcting imbalances of the electrolytes due to an excess of paraneoplastic hormone secretion does not make much sense if the patient is mindless from the uncontrollable effects of brain metastases. At best even if we treat the conditions listed in Table 25 vigorously, we should not expect to salvage someone for more than 6-12 months.

Spinal cord compression is almost always heralded by the prodrome of central back pain with or without radicular pain. The pain may be referred to the chest or abdomen and can be mistaken for non-malignant visceral disease such as pleuritis, pancreatitis, etc. Motor dysfunction often precedes paresthesia but they can occur simultaneously. Sensory changes are almost universally present before the development of paraplegia.

The majority of cases of superior vena caval syndrome occur in patients with primary lung cancers (85%); however, about 10% are due to malignant

TABLE 25

PALLIATIVE IMPERATIVE: ONCOLOGIC EMERGENCIES		
<i>Emergency</i>	<i>Cause</i>	<i>Therapy</i>
Increased Intra-cranial Pressure	Edema 2° Tumor	Corticosteroids Radiotherapy Fluid Restriction
Spinal Cord Compression	Tumor Compressing Spinal Cord	Corticosteroids Radiotherapy vs. Surgery
Superior Vena Caval Syndrome	Tumor Obstructing SVC Flow	Diuretic Corticosteroids Radiotherapy
Hyponatremia	Inappropriate ADH esp. with Oat Cell Cancer of Lung	Fluid Restriction Demeclocycline
Hypercalcemia	PTH, 2° Tumor esp. when Metastatic to Bone	Furosemide, NaCl Mithramycin

lymphomas and here the prognosis is often quite good. Rapid diagnosis is important before therapy begins so the proper treatment can be planned. Occasionally, one must treat without tissue diagnosis. If the irradiated tissue was the only obvious tumor mass, subsequent biopsy may be inconclusive. Laryngospasm is a dreaded complication.

Severe hyponatremia is seen in the inappropriate ADH syndrome, most commonly associated with bronchogenic carcinomas, especially oat cell cancers. Correction is eventually accomplished by control of

TABLE 26

**PALLIATIVE IMPERATIVE:
CANCER TREATMENT SIDE EFFECTS**

<i>Sign/Symptom</i>	<i>Possible Causes</i>
Abdominal Pain	GI Obstruction 2° surgical adhesions
Change of Bowel Function	
Ileus	Vincristine Toxicity
Thrombocytopenia	Chemotherapy (Radiotherapy) Rule Out DIC
Neutropenia	Chemotherapy (Radiotherapy)
Infection	Neutropenia 2° above
Congestive Heart Failure	Adriamycin Toxicity + Chest Radiotherapy Salt Retention 2° Hormone Therapy (Estrogens, Androgens)
Hypercalcemia	Hormone Therapy in patients with boney metastases
Pneumonitis (Pulmonary Toxicity)	Bleomycin Toxicity ± Lung Radiotherapy
Hematuria	Cyclophosphamide Therapy
Pericarditis	Left Chest Irradiation
Mucositis	Methotrexate Toxicity
Hepatotoxicity (Jaundice, Abnormal Liver Function Tests)	Methotrexate Toxicity Androgen Therapy
Nephrotoxicity (Decreased Creatinine Clearance, BUN Creatinine)	cis-Platinum Therapy
Esophagitis	Chest Irradiation ± Adriamycin
Proctitis/Colitis	Pelvic Irradiation

the primary tumor by appropriate therapy. Immediate correction is simply fluid restriction. Demeclocycline may be of benefit in refractory cases. Symptoms include extreme weakness.

Hypercalcemia is usually encountered in patients with widespread bony metastases from such common cancers as breast and prostate. It may, however, be seen in the absence of bony metastases in head and neck cancer and in some lymphomas. Other hypercalcemia-prone tumors are lung cancer and renal cell carcinomas. A hypercalcemic episode may be seen in up to 50% of the above mentioned cancers. It implies a limited prognosis of 6-12 months survival. Common symptoms are nausea, vomiting, constipation, urinary frequency, and dehydration. Less common are apathy, depression, fatigue, and weakness.

XI. SIGNS AND SYMPTOMS: IN PREVIOUSLY DIAGNOSED CANCER PATIENTS

While the uncured cancer patient has limited opportunity for long survival, the quality of short-term survival can be greatly affected by the physician's wisdom, diligence and humanism. The most important issues are often not whether the doctor recognizes the symptom or sign but whether something should be done about it. Successful treatment

of most of the oncologic emergencies may confer perhaps 6-12 months more of life. Whether the quality of that survival is worth the emergency measure is a matter for the patient, family and physician to ponder at leisure *before* the emergency arises. Good palliative care can be a source of pride and pleasure for patient, family and physician.

Attention to minute details or potentially dangerous symptoms can mean the difference between pathologic fracture of the hip or prophylactic elective radiotherapy. Any cancer patient with pain in a weight bearing area should have a plain x-ray of the area in question. If the cortex is seen to be involved, radiotherapy and orthopedic opinions should be obtained without delay. Pre-fracture therapy is much preferred. In patients whose cancers frequently involve bone such as prostate, breast, kidney, neck, and lung, a high level of suspicion should be maintained regarding any bone pain in weight bearing areas.

Sadly, some cancer patients complain of pain much too long when the concerned suspicious physician could easily diagnose bone involvement and prescribe the appropriate therapy, often localized radiotherapy which offers excellent relief in most circumstances.

Patients being treated for their cancers are subject to numerous unwelcome side effects of that therapy. Surgery, radiotherapy and chemotherapy all present patients with unpleasant sundry problems. If a cancer patient is undergoing or has undergone any of these treatment modalities, then the physician should be especially aware of certain important symptoms which would represent dangerous but treatable complications. See Table 26, for some of the commoner iatrogenic problems.

Even if cancer patients have been "cured" of their original cancer, one must remain vigilant to the possibility of a second cancer. Some are related to an inherent risk conferred by the first cancer. For example, a patient who has had breast cancer is more apt to develop a uterine cancer than a non-breast cancer patient. Further, second cancers may be caused by the "curative" therapy especially if it is chemotherapy or radiotherapy. The common notion that there is "only one cancer to a person" is quite untrue. Some folks get more than their share. Their physicians should remain alert to this possibility (see Table 16 and section, *II. CANCERS ASSOCIATED WITH OTHER CANCERS*).

XII. CONCLUDING REMARKS

One should never overlook the possibility that the patient has a curable cancer. Even if cure is not possible, significant improvement in survival is a reality for many cancer patients if properly and appropriately treated. Some tumors yield readily to good control and long survival, even when quite advanced. These include the lymphomas, breast cancer, germ cell tumors, and prostatic cancers. Consider also the marked (though short term) improvement in survival

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Officers Elected at the 127th Annual Session of the Maine Medical Association

Dixville Notch, NH • June 12-15, 1980

President

ROBERT E. MCAFEE, M.D.
Portland

Robert E. McAfee, M.D., of Portland, Maine, became the 131st President of the Maine Medical Association at the 127th annual session banquet on June 14, 1980. He served as President-elect of the Maine Medical Association from 1979-1980.



Dr. McAfee was born in Portland, Maine on August 25, 1935, son of Harold G. and Elizabeth H. McAfee. He was graduated from Deering High School in 1952, Bates College in 1956 and received his medical degree from Tufts University School of Medicine in 1960. He interned at the Maine Medical Center and served a residency in General Surgery from 1961 to 1965. Since 1965, Dr. McAfee has been attending surgeon at the Maine Medical Center and the Mercy Hospital, where he has been chief of surgery since 1974.

He is a member of the Cumberland County Medical Society, the Maine Medical Association, the American Medical Association, and is certified by the American Board of General Surgery. He is a Past President of the CCMS.

Dr. McAfee was formerly President of the American Cancer Society, Maine Division, Inc., Chairman of its Medical Affairs Committee and is currently a member of the National Board of Directors; was Chairman of the State Advisory Committee and State Ambulance Licensure Board of the Emergency Medical Services Division, Department of Health and Welfare; is a long-time member of the Committee on Recruitment, Aid and Placement of the M.M.A., serving as Chairman for several years; and is Chairman of the M.M.A.'s Long-Range Planning Committee.

Dr. McAfee served as Alternate Delegate to the AMA from 1972 to 1974 and has been Delegate to the AMA since 1974. He was re-elected to serve another term from Jan. 1, 1980 to Dec. 31, 1981. He is Chairman of the New England delegation and member and current Vice Chairman of the AMA Council on Long-Range Planning.

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ESOPHAGEAL PERFORATION: SOME GUIDELINES FOR DIAGNOSIS AND MANAGEMENT

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virulence of the inoculum can be reckoned with certainty.

The medical-legal liability for esophageal perforation has been reviewed by Holder.⁶ Among this lawyer's findings: 1.) *Res ipsa loquitur* is inapplicable, the courts recognizing the concept of "unavoidable accident." 2.) At least one surgeon was held liable for the nonoperative management of a small tear which later merited three operations. 3.) Perforation is so infrequent that the surgeon is *not* obliged to discuss the risk. This generally mild legal forecast belies the current malpractice climate and, in the author's opinion, prudence still dictates discussion with each patient to frustrate even a nuisance

charge based on uninformed consent.

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DIAGNOSTIC IMPERATIVES IN INTERNAL MEDICINE—Continued from Page 292

figures for oat cell carcinoma of the lung. Once universally lethal in 6 months, median survival for all aggressively treated patients is now 12 months. For those diagnosed in local stages, aggressive chemotherapy programs result in an increase of the median survival to 24 months. For some tumors, Hodgkin's, lymphoma and germ cell tumor, even an advanced stage is not incompatible with "cure." Their diagnosis should therefore never be missed.

The diagnostic imperatives in cancer span several different stages of disease. The most important group is asymptomatic patients in whom early

diagnosis will yield the highest cure rate. But even in symptomatic cases where the chances of cure seem less critical, one should pursue the diagnosis to be sure that curative procedures are not appropriate. One should also remember that there are tumors which even though advanced at the time of presentation, can be well controlled, and can yield long, good quality survival. Some may even still be curable. Finally, even in those cancer patients whose future is limited, prompt diagnosis of certain symptoms may yield important palliative gains, in which painful dysfunctional problems are avoided, or minimized.

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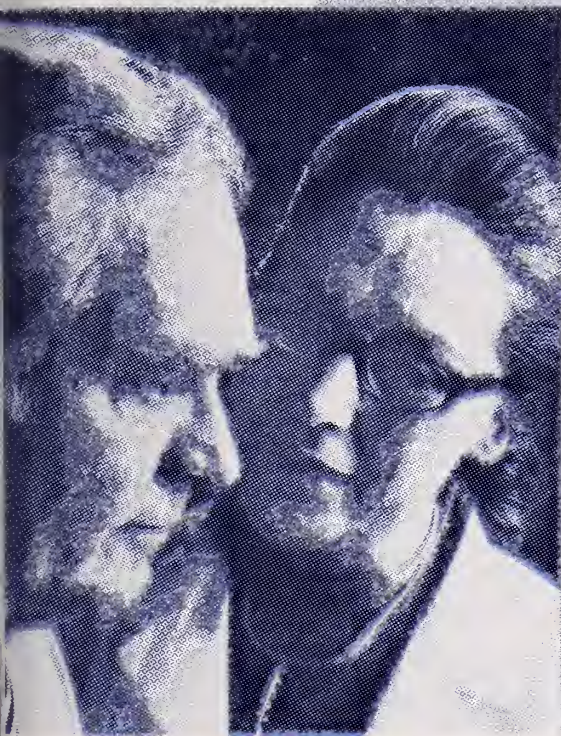


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ASYMMETRIC CRYING FACIES: A Possible Marker for Congenital Malformations

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Failure to consider this lesion in the differential diagnosis of neck masses can result in extreme hemorrhage when the lesion is biopsied.

Neck pain may be caused by musculoskeletal inflammatory conditions, tumors which have left the confines of a lymph node, and vascular disease. In the case of head and neck injury, especially from motor vehicle accidents, the cervical spine must be x-rayed because upper cervical vertebral fractures frequently coexist with facial, laryngeal, or neck injuries. In cases of neck pain that defy diagnosis, the physician should be alert to the possibility of carotodynia. This is a condition which, although not serious, often escapes diagnosis. It is characterized by chronic pain in the side of the neck and an absence of systemic symptoms or signs: the patient may tend to tilt his neck toward the side of the pain. The cause of carotodynia is unknown, but it is usually seen in patients with either a personal or family history of typical migraine. Diagnosis is easily made from the history and from finding an exquisitely tender carotid artery.

In the case of blunt injuries to the neck, the physician must be on the alert for a possible laryngotracheal fracture. Such an injury may result in rapid airway obstruction and, if the patient survives, in permanent voice and airway problems. Prompt recognition of the injury and proper surgical realignment of the displaced fragments of cartilage with stenting of the lumen and trachea may succeed in preserving a normal airway and normal laryngeal function.



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Pseudoseizures in Children

Presentation of Two Cases and a Discussion of Selected Diagnostic and Therapeutic Features

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The fact that psychological factors may be involved in the etiology of certain seizures has been recognized for more than a century.¹ Early reports by neurologists, such as Gowers² and Charcot³ described a phenomenon of "hysteroid convulsions" or *hystero-epilepsie*, which they distinguished from true epilepsy. Although the term hysterical seizure continues to be used by some authors to describe seizures which are felt to be psychogenic in origin,⁴ recognition that such seizures need not conform to traditional criteria for hysterical conversion or dissociative disorders has led to increasing use of other descriptive terms. The most common term in current usage is pseudoepileptic seizure, or simply pseudoseizure.⁵⁻⁷ Liske originally defined a pseudoseizure as "a clinical event which superficially resembles an epileptic attack, but, under close scrutiny, is found lacking in an essential epileptic component...or possessing a feature not compatible with epilepsy."⁵ That definition seems appropriate in that it acknowledges that such attacks are different from neurogenic seizures, yet does not attribute a single psychological mechanism to them.

The etiologic factors involved in pseudoseizures are not entirely clear, and almost certainly there may be different mechanisms involved in different cases. The role of emotional and situational stress has been emphasized in most series,⁴⁻⁹ but stress is also known to be a possible precipitant of true seizures. Thus, it may be difficult at times to distinguish between psychogenic seizures and psychogenically triggered neurogenic seizures.¹¹ This can be a particularly difficult problem given the fact that pseudoseizures have a tendency to occur in patients who have true seizures^{7,11} or other evidence of organic neurological

dysfunction.⁹ They also tend to occur in persons with evidence of psychopathology as shown through psychological tests such as the MMPI.^{6,9} Although some cases of pseudoseizures seem to represent true hysterical personality disorders, other proposed mechanisms for such attacks include anxiety attacks, hyperventilation, conditioned responses, and malingering.^{5,6} These other mechanisms are probably particularly important in children with pseudoseizures, since true hysteria seems to be less common in this group of patients.

Many authors have offered suggestions to aid the practitioner in clinically distinguishing pseudoseizures from neurogenic seizures.^{2,5-8} Gowers' original observations remain useful in this regard. He listed approximately a dozen characteristics which he felt distinguished the two groups. Features favoring a diagnosis of pseudoseizures over true seizures included: 1) more gradual onset, often with a "warning" before the seizure; 2) lack of definite pattern to the movements; 3) frequent vocalization during the seizure; 4) seizures last more than five minutes; 5) injury is uncommon ("the patient falls to the ground but rarely with the violence with which an epileptic falls"); 6) alteration rather than complete loss of consciousness; 7) urinary or fecal incontinence is uncommon; 8) induced termination of the seizure is often possible. Several authors have noted a tendency for rather dramatic flailing or struggling movements during a pseudoseizure,⁵⁻⁸ and some have pointed out that the movements frequently appear to have a purposeful element.^{7,8} In addition, pseudoseizures generally are not followed by a period of postictal somnolence, and there may be some preservation of memory for the event.^{7,8} One author reminds us that the patient is apneic during a true generalized seizure;⁷ he proposes that the response to artificial blockage of the airway during a seizure is a useful

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test—if the seizure stops or the patient resists the seizure is not epileptic. Finally, the EEG can be used to aid in the diagnosis. Using a continuous tracing during the seizure itself, a non-paroxysmal tracing is said to effectively exclude a neurogenic mechanism for that seizure,⁵⁻⁷ although there is a high incidence of other non-specific EEG abnormalities in patients with pseudoseizures.^{6,9,10} In spite of this, several authors make the point that the diagnosis of pseudoseizures is best made on clinical grounds using observational and historical features.⁶⁻⁸ Finlayson properly reminds us that investigation of possible psychosocial factors is a necessary step in the evaluation of atypical or suspicious seizure disorder and may facilitate accurate diagnosis.⁶

Once pseudoseizures have been recognized, a variety of treatment methods have been suggested for their management. Generally these have been one or more techniques of psychotherapy. Many series do not specify the techniques used but imply that traditional psychiatric methods were employed, with treatment of many cases extending over several months.^{4,5,6,8} In these series, older patients appear to have required or received longer courses of psychotherapy than children. Some series have described treatment using techniques of behavior modification, and there are a number of reports of success with this approach in children.^{5,11,12} Other techniques successfully utilized include hypnosis, self-control, family therapy, insight therapy, relaxation therapy, and biofeedback. Mostofsky has recently reviewed the range of psychobiological approaches to management of seizures.¹² One important point made by the same group in another discussion is the fact that psychological management may prove useful even in seizure disorders which are not purely psychogenic.¹¹

Most reports of pseudoseizures have concentrated on adult or adolescent patients, and one gains the impression that pseudoseizures are less common in the younger age group. Certainly less has been written about details of therapy in the younger age groups. Nonetheless, pseudoseizures can occur in pre-pubertal children, and there are at least a few such cases in some series, the group treated by Finlayson at the Mayo Clinic being the largest of the published series.^{6,11} Because pseudoseizures are perhaps more likely to be underdiagnosed in younger children, we present here two cases occurring in latency-age females. We hope that they will serve as a reminder that such cases may be encountered with some frequency in clinical practice.

CASE PRESENTATIONS

Two children found to have pseudoseizures were seen within a single year in a rural pediatric practice and were evaluated and treated with the aid of a clinical psychologist.

Case 1

"Gail" is a 10-year-old girl in the fourth grade who had her first seizure at 7 years of age. That seizure reportedly consisted of a period of staring, nonresponsiveness, chewing and gurgling motions, and right-sided facial twitching. One week later she had a

five-minute episode of staring and arm movements. A diagnosis of psychomotor seizure disorder was made by her physician at that time, and she was placed on diphenylhydantoin, which was later changed to phenobarbital; both medications were taken only inconsistently over the next three years. During that time she had three further seizures, each consisting of a several minute episode of staring, chewing and gurgling, and loss of awareness, followed by a brief period of confusion and dysarthria. An EEG done a year before presentation to this center was read as normal.

At the time of presentation, Gail had experienced a rapid increase in seizure frequency over a period of several weeks, and many of her seizures were of a different type than those which had occurred previously. Most of the seizures occurred at school, sometimes on a daily basis, and followed a similar pattern. Gail would have an aura of a globus-like sensation in her throat and then fall to the ground and shake and gurgle for several minutes, after which she would become alert but complain of a headache. Some of her spells showed minor variations in the pattern; for example, in some she would fall to the floor and appear to be limp and incoherent. In others she would scream, thrash about, struggle with observers, and bite her lip. Of note, she seemed to have some memory of the spells, and her mother felt that she could sometimes terminate a spell through talking to Gail re-assuringly. One of these agitated episodes was observed by a physician, and he noted that Gail was able to reach out to prevent herself from falling off a stretcher during the event. All of these spells occurred in the face of therapeutic serum levels of phenobarbital and in spite of the addition of diphenylhydantoin to therapeutic levels. Repeat EEG showed no focal abnormalities but was read as mildly abnormal "due to a non-specific increase in fast and slow activity."

During the period of increasing episodes, the possibility that some of these events might represent pseudoseizures was considered because of the following characteristics: increasing seizure activity in the face of increasing medication, after previous good control; the fact that she began to have several different patterns of seizures within a short period of time; the fact that seizures were preceded by an aura (globus sensation in throat); the tendency for seizures to occur mainly in stressful situations; the occurrence of purposeful behavior (prevention of a fall) during a seizure; the fact that some seizures could be terminated through parental actions; at least partial memory for some of the seizures; and absence of postictal phenomena. These features, together with a history of significant stress at school and home, led to a tentative diagnosis of pseudoseizures superimposed upon an underlying complex partial (psychomotor) seizure disorder. She was started on carbamazepine for the true seizures, and psychological consultation was obtained regarding the pseudoseizures.

Upon referral for psychological consultation, the social history was initially explored, the purpose being to elucidate the dynamics underlying Gail's pseudoseizures. The history revealed that Gail had experienced an acute increase in school-related stress, in the form of final exams and standardized achievement tests, at about the time her pseudoseizures emerged. It was noted that Gail was highly invested in school success and reportedly became increasingly anxious during the period of year end testing. While this factor may have been the trigger for the pseudoseizures, further examination revealed she was experiencing considerable chronic stress related to her family environment. This was associated with parental marital stress, sibling conflict over parental attention, and a pronounced feeling on Gail's part that she was not receiving adequate nurturance from either parents or siblings. She was also quite fearful that her seizures were potentially harmful to her. Gail became the focus of considerable familial concern because of her seizures, both on the part of the extended family members as well as the immediate family. Thus, attention seeking emerged as a general dynamic, with more specific emotional factors being the unmet nurturance needs, feelings of insecurity, a rivalrous need to achieve a stable relationship status in the family network, fears of school failure, and an acute increase in anxiety.

Based on these primary dynamics, the psychotherapy treatment plan emphasized three major elements: to provide Gail and her mother with an insightful understanding of the dynamics of the pseudoseizures; behavioral intervention strategies; and supportive counseling to Gail and her mother. Goals were to reduce acute anxiety, help parents develop more effective ways of expressing

nurturance and building family security, reduce inadvertent reinforcement of pseudoseizure behavior, reward non-seizure behavior, and facilitate Gail's self-control of her "spells." The treatment plan was implemented in a combination of individual and joint meetings, fourteen in all, with Gail and her mother.

The frequency of seizure-like episodes of all types diminished during the first three weeks of counseling, and by the fourth week Gail became symptom-free. She has had no more pseudoseizures from that time to the present, a period of about one year, nor has she had any further complex partial seizures; she remains on carbamazepine as her only medication. As improvement occurred, direct reinforcement of non-seizure behavior was made through rewards such as day camp and sleeping over with friends. Simultaneously, efforts by the family to provide attention and nurturance for non-seizure behavior further reinforced this adaptive, self-controlling behavior and reduced inappropriate attention-seeking.

Case 2

"Heather" is an 8-year-old girl in the second grade who had a first generalized tonic-clonic seizure at the age of six years. Her past health had been good. Family history revealed a history of generalized seizures in her natural father. An EEG was done at that time and showed background slowing but no focal or paroxysmal features. She was started on diphenylhydantoin and had good control of seizures for the next two years until the time of her presentation to this pediatric practice.

She was seen by the physician following two brief, typical tonic-clonic seizures and phenobarbital was added to her previous regimen. The following day she had six more generalized seizures and medication doses were increased. Serum levels several days later confirmed therapeutic levels of both anticonvulsants. Over the next two weeks she had a steady increase in the number of seizures, having as many as a dozen some days. At the same time, there was a change in the character of the seizures. Those occurring on the first several days involved loss of position, unresponsiveness, tonic-clonic movements of arms and legs, upturned eyes, urinary incontinence, and were followed by a period of lethargy and sleep. Subsequent seizures were far more dramatic and had several characteristics which raised the possibility of pseudoseizures, including the following: rather than typical tonic-clonic movements she had flailing, writhing, or random movements during these attacks; she cried out during some of the episodes; there was no post-seizure drowsiness; the seizures invariably occurred in settings where many people were present and drew considerable attention; she often would predict the occurrence of a seizure and on a few occasions was able to move to another part of the room before the seizure occurred; during at least one seizure she was partially responsive and was able to be roused from the seizure by a physician; the rapid increase in number of seizures occurred while her serum levels of anticonvulsants were in the therapeutic range. Recognition of the nature of these seizures was initially delayed by the typically epileptic features of the original seizures and the fact that the later seizures were not witnessed by a physician until one or two weeks had passed. When one such seizure was observed by a physician, the diagnosis of pseudoseizures was correctly made and psychological consultation obtained. Unfortunately, only a single meeting with the psychologist took place, but the course of that encounter is instructive.

Psychological consultation following the increase in seizure behavior and diagnosis of pseudoseizures revealed a recent family crisis in the form of the mother terminating her relationship with her boyfriend. The history further revealed that the family had moved three times over the past year, each time necessitating a school change for Heather, and that at the time of her seizures they were living in a large extended family situation on a temporary basis. It was noted that there had been a coincidental increase in Heather's clinging and attention seeking behavior with her mother at this same time. In this single contact with Heather and her mother, Heather presented provocative, manipulative, and seductive attention seeking behaviors such as wanting to sit on her mother's lap, clinging to mother, pouting dramatically, saying no one loved her or believed her seizures were real, denying emotional stress, feigning anger at mother, and demonstrating oppositional

behavior. She rejected all attempts by mother and the therapist to be supportive, which had the effect of frustrating and "hooking" mother into Heather's attention seeking pattern. The therapist stated clearly that no judgment regarding the authenticity of her seizure behavior would be made, only that efforts would be made to help overcome the problem.

Consultation with mother focused quickly on the apparent family crisis and associated emotional dynamics, the goal being to give mother insight and provide her with support for implementing behavioral intervention strategies. Mother was briefly instructed as to possible techniques for reinforcing nonseizure behavior and increasing noncontingent attention and nurturance, the goal being to provide for Heather's emotional needs without having her resort to such extreme behavior as represented by the pseudoseizures. Although a second meeting was scheduled, the family failed to follow up and contact was lost. Heather was seen for an unrelated medical problem several months later, and it was discovered at that time that she had experienced cessation of all seizure-like activity after the first session and had had no recurrences.

In this case, attention seeking was again a prominent feature, as was a precipitating emotional crisis. It was apparent that nurturance, security, and separation issues were involved. Heather's behavior reflected emotional immaturity and what could be described as hysterical features. Her behavior also had passive-aggressive qualities, manifested through resistance and opposition, with the apparent aim of tying mother more closely to her. The subsequent chance meeting revealed that although the pseudoseizures ceased abruptly after the consultation, Heather continued to utilize other attention seeking behavior with her mother.

DISCUSSION

As usually is the case in seizure disorders, both of the children described first came to the attention of the physician. Both children had been previously evaluated and treated for a seizure problem, and each was on a therapeutic regimen of anticonvulsant medication. Each had experienced authentic epileptic seizures prior to the onset of pseudoseizures, and each had experienced some kind of acute emotional stress immediately prior to the onset of the rapid increase in seizure-like behavior. In each case, evaluation of seizures by the physician revealed several features felt to be inconsistent with true seizures, which led to prompt psychological consultation.

From a psychodynamic perspective, the two case reports reveal several similarities. Each youngster was responding to preceptions of unmet nurturance needs and feelings of insecurity generated by family instability of some degree, and there was a corresponding effort to achieve attention from significant others. The pseudoseizures appeared in part to be a learned behavioral response which clearly would not be ignored, particularly in light of past neurogenic seizures, thus assuring that attention would be gained. While attention seeking and security needs characterized Gail's behavior, Heather more clearly evidenced emotional immaturity, dependence, and the hysterical features more commonly observed in certain adults manifesting pseudoseizures.

An important consideration in the diagnosis and treatment of pseudoseizures in children is the developmental level at which dynamics and symptoms are manifested. Obviously, young children rely more heavily on behavior and actions to express emotional needs, whereas adults are likely to manifest such symptoms in combination with more sophisti-

cated intellectualized, neurotic, hysterical and verbally articulated behaviors. Thus, one should be sensitive to the emotional dynamics of a child's behavior as an aid to understanding and diagnosing pseudo-seizures.

Another characteristic of the cases presented was the observation that secondary gain was achieved through the pseudoseizures. In each case the increased attention from family, physician, and therapist initially appeared to actually reinforce the pseudoseizure activity, leading to a further increase in frequency of the attacks. One practical implication of this is that increasing frequency of seizures during a period of increasing medical attention should alert the physician to the possibility of a psychological component to the disorder. In the two cases presented, psychotherapy appeared to have the effect of confronting secondary gains through inappropriate behaviors and restructuring delivery of emotional support through more adaptive channels.

In each of these cases, psychotherapeutic intervention emphasized a non-judgmental response to the seizure behavior, because of the real possibility that some of the seizures were neurogenic in origin. Instead, an effort was made to note that the problem of seizure behavior existed and that the therapist was going to assist the physician and family in trying to ameliorate this disorder.

In these two cases, the psychotherapy focused on several primary, but overlapping issues. In each case, a family centered approach was emphasized which addressed the family and environmental stresses. Secondly, efforts were made to delineate likely underlying emotional dynamics related to these stresses, the goal being to help the parents understand the probable causes of the pseudoseizures. Such insight and understanding is often helpful in supporting a parent's efforts to implement change. Third, a delineation of contingencies which triggered and maintained pseudoseizures was sought from which emerged strategies aimed at rewarding self-control and reinforcing non-seizure behavior while working to extinguish pseudoseizure behavior. This took the form of specific suggestions to parents and the children, such as rewarding non-seizure behavior with more freedom, more privileges, and special incentives. Finally, efforts were made by the therapist to provide a supportive, reality oriented helping relationship which offered encouragement, insight, and guidance on a regular and consistent basis. In Gail's case it seemed apparent that the amount of time offered for regular consultation enhanced her progress. This approach might generally be referred to as a cognitive-learning orientation, as both dynamic and behavior issues were addressed.

CONCLUSION

While the physician must remain alert to the appearance of true seizures, these cases highlight the importance of remaining sensitive to the possibility that emotional stress can and does contribute to seizure behavior. In the cases described above, emotional stress contributed to the onset of pseudoseizures which were relieved by emotional support from the family, physician, and therapist. If recognized promptly, pseudoseizures in children may be amenable to effective, rapid, and relatively uncomplicated intervention utilizing well established psychotherapeutic techniques. Early recognition can minimize toxicity from unneeded medications, obviate the need for expensive and potentially dangerous diagnostic procedures, and facilitate initiation of appropriate therapy.

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Therapeutic Embolization for Palliation of an Inoperable Renal Carcinoma

ROBERT BATE FUNCH, M.D., F.A.C.R.*

The new and rapidly growing field of therapeutic angiography may contribute to the management of the patient with renal carcinoma either pre-operatively or for the palliation of advanced or unresectable lesions. The very angiographic catheter used to confirm the diagnosis of a suspected kidney tumor may also become the vehicle for selective delivery of embolizing material. Pre-operative therapeutic embolization of the renal artery has the theoretical advantage of lowering the incidence of metastasis by reducing the number of tumor cells entering the venous circulation during surgical manipulation and the real advantage of facilitating surgery by minimizing blood loss, improving the delineation of dissection planes, permitting transection of the renal vein early in the dissection and shortening the length of operation. If radiation therapy is planned, it should precede embolization so that ischemia does not increase radio-resistance of the tumor.

In the symptomatic or asymptomatic patient with metastasis to the lung or bone, Chuang, et al have observed useful palliation and doubling of survival time when therapeutic embolization is followed in two weeks by delayed nephrectomy and hormonal treatment with Provera® but not in the patient with metastasis to the liver.

Finally, therapeutic embolization has been employed without subsequent surgery to palliate pain or bleeding in the inoperable patient with renal carcinoma as in the case reported below.

CASE REPORT

A 61-year-old, white female presented in March 1980 with the chief complaints of gross hematuria and back pain. Intravenous and retrograde urography revealed poor function of the right kidney and scanty visualization of a distorted collecting system associated with a huge mass, measuring over ten cm., occupying the upper two-thirds of the kidney. There was a focal hydronephrosis of the upper pole of the left kidney proximal to an inflammatory stricture of the infundibulum of the upper pole collecting system. On the second day after admission, mid stream aortography, selective right renal arteriography, selective right renal venography, and inferior venacavography were carried out by percutaneous technique through the left femoral artery and vein. The angiographic findings (Fig. 1) were those of a tumor invading most of the kidney, except the lower pole, with the typical malignant neovasculature of renal carcinoma. The renal vein was completely occluded (Fig. 2) and a three cm., spherical intraluminal mass filled the cava at the T-12/L-1 interspace level (Fig. 3). These evidences of tumor extension and embolization into the renal vein and proximal vena cava were accompanied by an additional three cm. mass deforming the left lateral wall of the cava below the renal vein insertion at L-2/L-3 level (Fig. 3) suggesting distal caval intravascular extension or caval invasion by metastasis to adjacent retroperitoneal lymph nodes. Carcinoembryonic antigen was 4 ng/ml, hematocrit 34, hemoglobin 10.5 gm.%, serum iron 35

mcg., T.I.B.C. 192 mcg. Urine analysis was 3+ for albumin, loaded with red blood cells, 200+ wbc/hpf, and urine culture was positive for *E. coli*. Sedimentation rate was 107 mm. per hour. Prothrombin time and P.T.T. were normal. SMA 12 was normal.

The angiographic diagnosis of malignancy and demonstration of transvenous spread were considered convincing evidence for inoperability and plans were made for percutaneous, transcatheter, therapeutic embolization of the right kidney through the single renal artery. While preparing for this treatment, hematuria increased and passage of blood clots was accompanied by severe renal colic. A week after the angiographic studies, percutaneous translumbar biopsy of the renal mass was performed with a 23 gauge Chiba needle confirming the diagnosis of renal carcinoma and followed immediately by the placement of a 5 French, polyethylene, non-tapered catheter into the right renal artery by percutaneous technique through the right femoral artery. Three Gianturco, 5 mm., steel, mini-coil occluding devices were delivered into the artery (Figs. 4, 5, 6) and complete occlusion promptly obtained (Fig. 5). The patient tolerated the procedure very well with only mild flank pain during the next two days. Fifteen mg. of morphine sulfate were titrated intravenously during the biopsy and embolization procedure. One hundred mg. of Nembutal® were required that night for sleep and Tylenol® was sufficient to control the discomfort the next day. The patient's temperature rose to 102.6°F the next day, 102°F the second day, 101°F the third day, and then returned to normal. There was no recurrence of renal colic, hematuria, or flank pain. Ampicillin was continued for the infection in the opposite kidney and the patient discharged afebrile ten days later. Within a few weeks pelvic pain was prominent and radiologic examination confirmed the clinical diagnosis of metastasis, revealing osteolytic metastases in the bony pelvis as well as pulmonary metastasis. At the time this report was submitted, the patient was alive as an outpatient nine weeks after the therapeutic embolization procedure with the pain of the bony metastases being controlled by oral morphine and without recurrence of the hematuria or flank pain.

DISCUSSION

Most surgeons now choose to electively embolize a very vascular hypernephroma pre-operatively. There are about 1500 new cases of carcinoma of the kidney diagnosed in the United States yearly and at least one-half of these patients will die from the disease. From one-quarter to one-half of the patients have metastases in the lung, liver, skeleton, or brain at the time of diagnosis. There will undoubtedly be an increasing demand on the interventional radiologist to perform this procedure on patients with both localized and disseminated disease.

The kidney is a favorable site for embolization because of its singular vascular supply and the relative ease of catheterization of this vessel. A variety of agents have been used for occlusion including mechanical devices, particles, and liquid tissue adhesives, each with its advantages and disadvantages.

The Gianturco coil is a five cm. long coiled steel wire to which strands of wool or Dacron are attached to induce thrombosis. The minicoil is a smaller version deliverable when straightened through a 5 French, non-tapered catheter. The most recent

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Fig. 1



Fig. 2



Fig. 3

Fig. 1. Spot film of right renal artery hand injection flush angiogram through 5 French, non-tapered catheter immediately before the therapeutic embolization. Typical, malignant neovascularity of renal carcinoma. Note the lower pole branch (arrows) into which the first coil was later anchored.

Fig. 2. Right renal venogram revealing complete obstruction of the renal vein.

Fig. 3. Inferior venacavogram. 3 cm., spherical, intraluminal mass filling the caval lumen at thoraco-lumbar interspace level. At L-2/L-3 interspace level a second 3 cm. mass deforms the left lateral caval wall well below the renal vein level.



Fig. 4a

Fig. 4a. Insertion of first Gianturco steel and Dacron minicoil into lower pole artery and peripheral segment of main renal artery.

Fig. 4b. Flush angiogram five minutes later. The lower pole artery is thrombosed but occlusion of vascular supply to rest of kidney is very incomplete.



Fig. 4b



Fig. 5a

Fig. 5a. Insertion of second coil into main renal artery.

Fig. 5b. Flush angiogram five minutes later reveals complete thrombosis of renal artery. A lumbar artery is filled from reflux back into the aorta.



Fig. 5b



Fig. 6a

Fig. 6a. Flush angiogram five minutes after third coil delivered into main renal artery. Complete occlusion. Successful embolization of the kidney.



Fig. 6b

Fig. 6b. Final appearance after complete removal of introducer, guide wires, and catheter.

modification is available in three mm., five mm., and eight mm. sizes and can be delivered through any tapered catheter that will accept a size 38 guide wire and accordingly will extend the usefulness of this device. These coils remain in place permanently and are able to evoke occlusion of large vascular structures with high flow rate. They are easily introduced and may be localized radiographically and are palpable at surgery. Their disadvantages include their dependence on the patient's clotting factors to produce the occlusion, inability to produce direct distal vessel occlusion, and difficulty in retrieving misplaced coils. With only proximal artery occlusion, peripheral collateral circulation may develop and, therefore, it is probably ideal to use a combination of

particulate occluding material for peripheral embolization followed by the permanent proximally placed coils when treating a vascular renal tumor.

The particles are inexpensive, readily available, and easy to use but have the disadvantages of being flow-directed and, therefore, less controllable, can pass through shunts to cause peripheral embolization, may reflux to undesirable sites, and most of them, with the notable exception of Ivalon, produce temporary occlusion. Commonly used particulate materials for embolization include autologous clot, Gelfoam®, and Ivalon®.

Tissue adhesives can be delivered through microcatheters, are permanent, and are independent of the

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Primary Biliary Cirrhosis and Scleroderma Variant

A Case Presentation

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The association of primary biliary cirrhosis and scleroderma variant (CREST syndrome) was first reported by Reynolds, et al.^{1,2} Since then there have been other articles^{3,4} in the literature dealing with the association of the two illnesses once thought to be two separate entities, now possibly related pathophysiologically. The following case is a review of an elderly lady with CREST syndrome and primary biliary cirrhosis. The literature will be reviewed with regard to the current data supporting a link between these two diseases.

CASE REPORT

The patient is a seventy-seven-year-old white female who presented for a routine evaluation in 1974. At that time her only complaint was that her hands would become very red at times and also blue, depending on the temperature outside, and would occasionally swell. This had been a problem for many years. Early in life her fingers would turn white with cold exposure and then red on warming. She had no significant past medical problems, except for surgery, which included an appendectomy and a cholecystectomy. She did have some trouble with leg ulcers in the early '60's. Her alcohol consumption had been one to two drinks a day with the quantity decreasing over the last three years. Her family history revealed that her father died of a heart attack and her mother died of metastatic cancer. She had only one sister who died of the Asian flu. The only significant findings on physical examination were telangiectasias on her hands, lips, feet, and a few scattered on all four extremities (Figs. 1, 2).

Over the next year she had occasional trouble with pruritis. Occasionally epistaxis occurred secondary to telangiectasia. She was seen again in August of 1975 for re-evaluation, at which time she was asymptomatic, but a routine SMA-12 revealed abnormal liver function tests (Table 1). A liver scan was normal. It was felt that a biopsy of the liver would be hazardous because of the telangiectasias, and no further evaluation was performed. She continued to remain asymptomatic until August of 1976 when blood was noted in her stool. A barium enema was performed showing giant diverticula compatible with scleroderma (Fig. 3). In September of 1977, she was seen for polyarthralgia. At that time her physical examination was normal, including no liver enlargement, and her joints appeared to be the joints of osteoarthritis.

In March of 1978, the patient presented with trouble swallowing food. A barium swallow was performed, and this showed depressed esophageal motility compatible with scleroderma. In addition, she had pulmonary function tests which showed a vital capacity of 76.5% of predicted with an FEV-1 which was normal (a restrictive pattern). Arterial blood gases showed a PO₂ of 78.1, a PCO₂ of 26.7, and pH of 7.44. In early October of '78, she began to have trouble with bronchospasm, which persisted for approximately six months. This finally responded to alternate-day prednisone therapy, which was subsequently withdrawn. This has not been a problem over the last year. During this episode she had a chest x-ray which showed some pleural thickening which has persisted.



Fig. 1



Fig. 2

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TABLE 1

LABORATORY DATA									
	SGOT	Chol.	Alkaline Phosphatase	Gamma-GT	C-4	C-3	IgM	ANA	Ratio
9/75	39	274	326	517					
8/77	37	312	297						
9/78	26		281		8	82	420	1:128	1:20480
5/79					9	111	220	1:32	1:320
5/80	38	224	283						
	Antimitochondrial								
5/79	1:128								
	Cryoprotein								
4/80	trace								



Fig. 3

In May of 1979, the patient was put into the hospital for an open liver biopsy. Histological sections through the liver showed monolobular fibrosis with fibrous bands extending around liver lobules. Cellular infiltrate consisted mainly of lymphocytes with a few plasma cells. The lymphocytic infiltrate was diffuse with occasional lymphoid follicle formation. The lymphocytes had invaded the limiting membrane and had given it an eroded appearance. The adjoining liver cells showed feathery degeneration. There was reduction in the number of small intrahepatic bile ducts. Focal proliferation resembling very small bile ducts was noted. There was no cholestasis. The histological findings were compatible with primary biliary cirrhosis (Fig. 4). During this hospitalization, she had an immunological evaluation which revealed an IgM of 220 mg., ANA of 32, latex fixation of 320, and an antimitochondrial

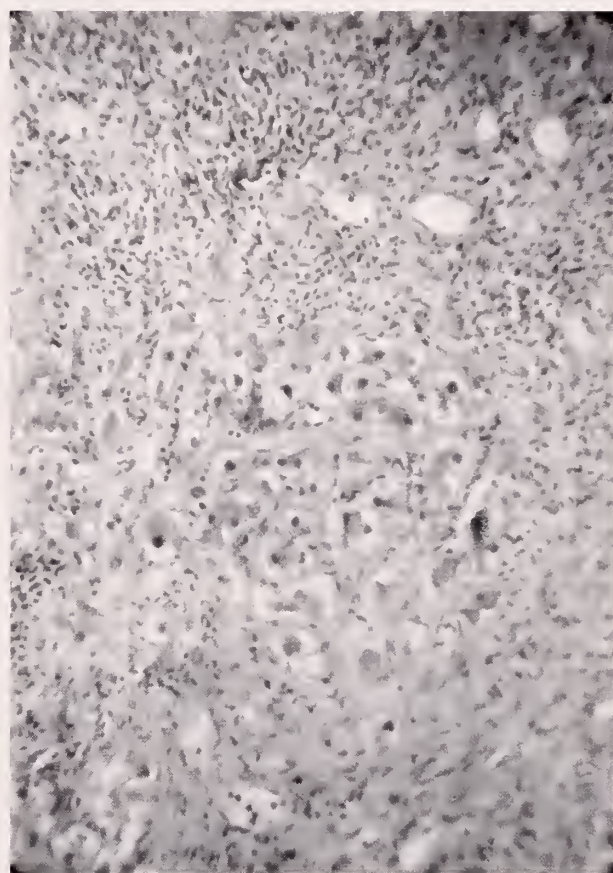


Fig. 4

antibody of 1:128. Her C-3 was 111 and C-4 was 9. In addition, she had trace levels of cryoproteins in her serum. Prior to May of 1979, she had an IgM value of 420, latex fixation of 1:20,480, ANA of 1:128, C-3 of 82, and C-4 of 8. These values were present in September of 1978 (Table 1). Since May of 1979, the patient has remained asymptomatic except for one more episode of G.I. bleeding. Her physical exam continues to be normal, except for occasional wheezing and the telangiectasias noted on her extremities and lips.

DISCUSSION

When first presenting, this patient appeared to have hereditary hemorrhagic telangiectasia, or Osler-

Weber-Rendu syndrome. However, as her clinical course progressed, it became obvious that we were not dealing with telangiectasia alone. Complications such as gastrointestinal bleeding and trouble swallowing occurred. It became apparent that she had several classic features of progressive systemic sclerosis. The esophageal motility abnormality and giant diverticula are seen frequently in this disease. In addition, she has a restrictive pattern on her pulmonary function tests and evidence of pleuritis. These findings are the most frequent pulmonary abnormalities of progressive systemic sclerosis.⁵ The elevated ANA and latex fixation are seen in this illness also. With regard to the CREST syndrome, there is no evidence of sclerodactyly or calcinosis by hand x-rays. It is felt that her current hand symptoms are secondary to edema due to the telangiectasias. However, she did have Raynaud's phenomenon in the past.

In summary, the patient has three features of the CREST syndrome and several features of progressive systemic sclerosis. Therefore, scleroderma variant is the most appropriate diagnosis for her collagen disease. Valayos, et al⁶ discuss the overlapping nature of the two diseases.

The data supporting primary biliary cirrhosis are the elevated IgM, borderline low C-3 and elevated ANA. In addition, an elevated antimitochondrial antibody is virtually diagnostic of this illness, and the patient's is 1:128.⁷ Finally, circulating cryoglobulins were found in her serum, which also is seen in most patients with primary biliary cirrhosis.^{8,9}

Histological diagnosis of primary biliary cirrhosis from too small a biopsy specimen is sometimes very difficult due to lack of inclusion of portal areas. Diagnostic features are seen more often in larger ductules which are included in open liver biopsies rather than percutaneous biopsies.¹⁰

The hepatic lesions are distinctive, but may be difficult to distinguish from chronic hepatitis and cryptogenic cirrhosis. Klatzkin and Kantor¹¹ suggested that mitochondrial antibodies provide a confirmatory evidence of primary biliary cirrhosis when biopsy findings are consistent.

In early stages, rupture of septal and interlobular biliary ducts and necrosis of epithelium are noted. The portal areas show infiltration by lymphocytes and plasma cells. Sometimes lymphoid follicles or epithelioid granulomas are noted. Although lobules are not affected, the limiting membranes may be disrupted. No cholestasis is noted in early stages. In later stages, the destruction of the portal ductules is pronounced. Focal proliferation of flat eosinophilic cells near the hepatic lobules is noted, and these appear to be bile ductules with atypical epithelium and absent luminae. Later on scarring sets in, and enlarged portal tracts containing arteries, veins and collagen, but no bile ductules are noted. This progresses to cirrhosis with scarcity of bile ducts. At this time cholestasis may be pronounced.¹²

The etiology of primary biliary cirrhosis remains

obscure, but there is a growing body of evidence suggesting some abnormality in the immunological system. Thom, et al⁸ note that large immune complexes are present in the serum of most patients with primary biliary cirrhosis in the form of cryoproteins composed primarily of IgM. This is supported by the work of Wands, et al,⁸ who have used the Raji cell immunoassay on twenty patients with primary biliary cirrhosis and found cryoprotein in ninety percent (60% IgM, 20% IgG-IgM, and 5% IgA-IgM). All complexes were capable of activating the complement system *in vitro*. It is theorized that the large complexes could be formed in the vicinity of bile ducts by an antigen absorbed from bile or biliary epithelium. In support of this is the finding of IgM forming plasma cells around bile ducts being destroyed.¹³ Also, anti-bile canaliculi antibodies have been found recently.¹³ Although antimitochondrial antibodies are very specific for primary biliary cirrhosis, these antibodies are not specific for liver mitochondria.¹³

Jones, et al¹⁴ have noted a hypercatabolism of C₃, suggesting chronic complement activation. In addition, they have observed a defect in clearance of sensitized erythrocytes by receptors C_{3b} on Kupffer cells. Possibly this is secondary to a large portion of these receptors being occupied either by immune complexes containing C_{3b} or excessive C_{3b} that is being generated by complement activation. These abnormalities were not observed in Hbs-antigen negative chronic active hepatitis.

Although the above is rather convincing evidence for an immunological mechanism for primary biliary cirrhosis, there is another theory offered by Miller, et al.¹⁵ They don't feel that the above data is convincing and offer another etiology for primary biliary cirrhosis. They have noted that patients with primary biliary cirrhosis or progressive systemic sclerosis have lymphocytes that can be induced to release migratory inhibitory factor after exposure to mitochondria. This suggests a sensitization to cell mitochondria. Possibly these same sensitized lymphocytes may yield collagen accumulation inappropriately through lymphokine stimulation.

If we are dealing with an immunological etiology for primary biliary cirrhosis, then one can realize why the association with collagen diseases occurs. Sjogren's syndrome is the most common systemic immunological disease associated with primary biliary cirrhosis.¹⁶ Progressive systemic sclerosis and/or CREST syndrome is the next most common associated immunological disease.¹ Finally, rheumatoid arthritis, systemic lupus erythematosus, interstitial pneumonitis, and thyroiditis have rarely been associated with primary biliary cirrhosis. All these diseases have associated immunological abnormalities and altered immune responses to a varying degree. It is possible that the immune complexes initiated in the liver reach the systemic circulation and cause the systemic illness. Most likely we are dealing with a primary insult (i.e., viral or bacterial

infection) that initiates an abnormal immunological response in a patient genetically predisposed to develop one or more of the above illnesses. In fact, there is a high frequency of the genetic foci HLA-A1 and B-8 in progressive sclerosis and primary biliary cirrhosis.⁴

Therapeutically, there are two approaches that show promise. Epstein, et al¹⁷ have treated several patients who have primary biliary cirrhosis with D-penicillamine for twelve to twenty-four months with a decrease in IgG, IgA, and IgM levels. These patients had a decrease in the rate of rise of bilirubin compared with controls. In addition to lowering immunoglobulins, D-penicillamine may help by its copper chelating action in the liver.

Finally, Ericksson and Lindgren¹⁸ have treated five patients with primary biliary cirrhosis and progressive systemic sclerosis by chronic plasma exchange. They have shown an improvement in lung diffusion capacity in one patient, and in all the IgM levels and cryoprotein levels have fallen. It is possible that in the long run this therapy may remove these complexes from the Kupffer cells and improve hepatocyte function. They have not shown this affect as of this writing.

In summary, a case of primary biliary cirrhosis and scleroderma variant has been presented. The patient is currently doing well on no therapy, supporting the chronicity of this problem and possibly the more benign nature of this combined disease in the elderly population. The current theories on the etiology of primary biliary cirrhosis have been reviewed. As with all the other autoimmune illnesses, we do not have a proven theory with regard to etiology although immune complexes seem to be a dominating factor in this illness. It is disconcerting that we cannot find an answer for the elevation in antimitochondrial an-

tibodies when it is a rather specific finding for primary biliary cirrhosis.

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patient's own clotting factors but the most promising example of this group, isobutyl 2 cyanoacrylate (Bucrylate), is not commercially available at this time.

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Asymmetric Crying Facies:

A Possible Marker for Congenital Malformations

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Screening for occult disease is important in child health care, and the association of single umbilical artery with renal anomalies represents an example of a minor physical finding that suggests the possibility of an otherwise unrecognized congenital malformation.¹ From 0.67% to 2.1% of newborns have significant congenital anomalies, and many of them are both occult and remediable.

This report describes an infant with asymmetric crying facies who also had vesico-ureteral reflux and congenital hip dysplasia. Others have suggested that asymmetric crying facies are usually due to unilateral congenital hypoplasia of the depressor anguli oris muscle (DAOM). Also, this lesion is said to point to the possible co-existence of a more serious congenital malformation. This report will examine the validity of the latter claim and make recommendations for evaluation of children with asymmetric crying facies.

CASE REPORT

L.B. presented at two months of age with bilateral otitis media. She was noted also to have asymmetric crying facies, which her mother had first observed at one week of age. The right angle of the mouth migrated inferiorly on crying while the left angle did not move. Both the right and left naso-labial folds were preserved. She had symmetric forehead wrinkling and eye closure. Her facial expression was normal when she was not crying, except for minor thinning of the lower lip vermilion on the left. Her hips abducted adequately and symmetrically, and no other signs of congenital dislocation of the hip were present.

At five months of age, after five days of intermittent fever, a catheterized urine sample yielded *E. Coli*, colony count greater than 10^5 . At seven months, an IVP was normal, but the voiding cystourethrogram showed "free reflux into a dilated left ureter and into the pelvocaliceal system of the left kidney." She has remained on prophylactic therapy with sulfisoxazole to her present age of 27 months. Multiple screening urine cultures have been negative.

An incidental finding on the IVP was an abnormal left hip. Pelvic radiographs showed mild dysplasia. She was treated with a Pavlik harness for six months, and radiographs at 24 months of age were normal. Her growth and development have been normal, and at 27 months of age the asymmetric crying facies remain unchanged (See Figure 1).

The patient had been the 3689 gram, full term product of an uncomplicated pregnancy, labor, and delivery, born to a twenty year old grav. 2, para 1 mother. Forceps were not used at delivery. The family history is negative for facial weakness or asymmetric facies. The paternal grandmother has probable left ureteral reflux, and a paternal first cousin had congenital dislocation of the hip.

DISCUSSION

Congenital hypoplasia of the DAOM is one of several possible causes of facial asymmetry in the newborn. A few children presented to neurologists with what was described as "limited facial weakness."² Biopsy studies showed absence or



Fig. 1

hypoplasia of the DAOM in some of these cases.³ Electrodiagnostic studies indicated that the facial nerve was intact in congenital hypoplasia of the DAOM, also called the quadratus labii inferioris muscle. The muscle originates from the oblique line of the mandible, extends superiorly and medially through the obicularis oris, and is attached to the skin and mucous membrane of the lower lip. It is innervated by buccal and mandibular branches of the seventh nerve. The muscle pulls down the ipsilateral, lower corner of the lip and everts it.⁴

One can distinguish congenital hypoplasia of the DAOM from other causes of facial asymmetry without resort to electrodiagnostic methods. Peripheral facial nerve paralysis is suggested by a history of obstetric trauma or by signs of upper and lower facial weakness. Facial asymmetry may be part of the hemifacial microsomia syndrome which includes either seventh nerve palsy or unilateral hypoplasia of facial muscles. In this instance, the asymmetry would be associated with other anomalies that are part of the first branchial arch syndrome. Hypoplasia or aplasia of the seventh nerve nucleus causes limitation of lower facial mobility, but this

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situation, part of the Moebius Syndrome, is rare, usually bilateral, and often associated with paralysis of the sixth cranial nerve. Facial palsy of supranuclear origin existing without other neurologic dysfunction is extraordinarily rare and should cause flattening of the naso-labial fold, which is not part of congenital hypoplasia of the DAOM. Another possibility would be that dysfunction of the DAOM is caused by denervation of the mandibular branch of the seventh nerve. However, this twig innervates the mentalis muscle in addition to the DAOM, and with asymmetric crying facies, the mentalis muscle continues to function despite dysfunction of the DAOM. We believe that the asymmetric crying facies in our patient represents congenital hypoplasia of the DAOM.

Asymmetric crying facies may be associated with other congenital anomalies. Caylor, a pediatric cardiologist, found fourteen cases of "unilateral partial facial weakness" associated with congenital heart disease.⁵ Twelve of the fourteen had a ventricular septal defect, and twelve of the fourteen had right sided facial weakness. Several had defects of other organ systems including vertebral and renal anomalies, plus congenital dislocation of the hip. He could find no etiology for the facial weakness and speculated that an infection of the fetus might have occurred in the first trimester, noting that embryologically the hyoid arch is close to the cardiac premordium. Of the ten children described by Nelson with congenital hypoplasia of the DAOM, two had congenital dislocation of the hip.⁶ Pape, studying a population of hospitalized children at a referral center, found forty-four children in one year with asymmetric crying facies.⁷ Thirty-four of them had associated congenital anomalies, twenty-seven of which were known prior to the study. Seven were discovered after recognition of asymmetric crying facies. Twenty of the children had right sided hypoplasia, twenty-four had left sided. The distribution of cardiac, genitourinary gastrointestinal, and musculoskeletal anomalies seemed to be equal between the right and left side. The laterality of the hypoplasia coincided in all but one instance with that of the unilateral anomalies. The authors did not distinguish hypoplasia of the DAOM from other causes of "partial facial paralysis."

Two prospective studies of asymmetric crying facies in newborns have been reported. In one series, the lesion was present in 41 of 4360 newborns (0.6%), in the other, 44 of 6487 (0.7%).^{8,9} In both studies, left sided hypoplasia predominated over right, 34 to 7 in one and 30 to 14 in the other. In the first series, congenital malformations were associated with asymmetric crying facies in two of 41 infants, in the other, 11 of 44. In the study showing few associated anomalies, the babies were not followed beyond the newborn nursery, and neither radiographic studies nor ECGs were performed. In the other series, the affected infants were followed for at least a year, with radiographic and electrocar-

diographic studies being performed. Also, electrodiagnostic studies were performed in fifteen babies in this series to establish the diagnosis of hypoplasia of the DAOM.¹⁰ In this group, three babies had ventricular septal defects, three had congenital dislocation of the hip, two had large hemangiomas, and one each had micrognathia, undescended testicle, and a supernumerary nipple. Of 6443 babies in the second series without hypoplasia of the DAOM, 2.7% had associated malformations. Of the affected babies, 20% had other defects. This comparison was made in the newborn nursery.

Hypoplasia of the DAOM may be familial. Three of 41 in Perlman's study and 17 of 37 in the series of Papadatos had other affected family members. A family has recently been described including a mother, her two children, her brother, and her father, all with asymmetric facies.¹¹ The authors suggest that congenital hypoplasia of the DAOM, if inherited, is unlikely to be associated with other defects. They speculate that the transmission of the inherited form of DAOM hypoplasia probably has variable penetrance which may account for the absence of associated lesions.

Our patient had all three of her anomalies on the left side. Others have pointed out the tendency of certain sets of malformations to be located on the same side. An example is the left side location of plagiocephaly, congenital dislocation of the hip, and the convexity of scoliosis, when all three co-exist.¹² Also, the laterality of unilateral malformations of paired structures apparently occurs in a non-random fashion; some anomalies are usually right sided, others, usually left sided.¹³ Lastly, our patient may be unique in that none of the other reports have included a patient with vesico-ureteral reflux coexisting with asymmetric crying facies.

The physician caring for a child with asymmetric crying facies should, we believe, be aware of the possible association of other congenital defects. These include congenital heart defects, skeletal anomalies, genitourinary lesions, and less commonly, gastrointestinal and neurological defects. How vigorously should these malformations be looked for? At the least the physician should perform, in our view, a complete history and physical examination along with tests such as urine cultures, chest and skeletal radiographs.

SUMMARY

We have reported a case of probable congenital hypoplasia of the DAOM with additional malformations—vesicoureteral reflux and congenital dysplasia of the hip. The literature was reviewed, especially that noting a possible relationship of asymmetric crying facies with other defects. We conclude that the association is probably real, and that one should actively seek out other possible malformations in the child with asymmetric crying facies.

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A Report on "Living with Cancer, Accent on Stress"

BERNARD T. PRICE, M.D.*

Cancer, as a word or a reality, has a strength that extends into every aspect of the lives of those it touches. It brings some unique stresses into the social, psychological, physical, and economic spheres of the lives of the patients and their families. The impact of cancer was the topic of the Conference, "Living with Cancer, Accent on Stress" on May 18 and 19, 1980 in Augusta, Maine. Approximately 300 patients, family members, and professionals came together to talk about those stresses.

The disease of cancer quickly becomes "A Family Affair," and Eric and Micki Esselystyn discussed how their own lives had been initially consumed by this disease. The patient-victim and the family-victim both suffered. Each became isolated, depressed and angry. No part of their lives, alone or as a couple, escaped the ravages of the disease. Their children were also deeply involved in their own anger and isolation. Through a series of happy occurrences, the Esselystyns found a way to use their own tragedy to turn it into a growth experience as a family. The walls of isolation dropped, and they grew together. The integral concept that allowed this growth was a process of daily freeing their energies once consumed by cancer's associated stresses and redirecting those energies toward life. They presented their own understanding of the Simontons' work in mental imagery and relaxation as their own method of dealing with the stresses they found in their lives. Those stresses that had led them initially to live conditionally and tentatively resulted in withdrawal and isolation. They found that by redirecting their life forces to make their own choices they freed themselves from the victim role.

Tony Montenaro and his mime troupe presented a series of skits that entertained and provoked thought. This was a lighter method, but many were able to identify with the ideas and to laugh.

After both the Esselystyns' presentation and the

mime, there were panel discussions. The panels were composed of patients and family members presenting their own stories and their feelings on what they had just seen or heard. This open session allowed people to discuss what was really important to them in their lives. In this sharing, there was a spirit of eagerness to help another human being. By the union of hands, the stresses of cancer could be diminished.

That spirit continued into the workshops where specific stress problems were addressed, and different methods of controlling stress were taught. The stresses discussed were those involving telling children about cancer and helping them cope, getting information from the doctor, and being discriminated against at work. Such diverse stress relieving methods as relaxation techniques, visualization, religion, and hospice care were discussed.

A major emphasis within this conference and workshop was directed at the self-help and support groups designed to help patients and their families. The traditional groups are well-known resources such as the Ostomy Association or Reach to Recovery. There are also new resources, such as support groups composed of mixtures of patients and families coming together to talk about their feelings. These groups are developing throughout the State, and are important for the emotional support they give to people dealing with cancer.

Cancer is a disease that leaves its mark within the emotions as well as within the body. The effects on the family and on the patient extend far beyond the biologic processes of the disease. This conference was an important one, because from it people throughout the State came together and shared of themselves. The grass-roots process of self-help groups that had already begun has multiplied. There is a new hope to share, and by that sharing to relieve some of the pressures of "living with cancer."

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Diagnostic Imperatives in Internal Medicine

The Timely Detection of Treatable Disease

Otolaryngology

WERNER D. CHASIN, M.D.*

Mild disorders affecting the ear, nose, throat, and their adjacent structures are very common; more serious conditions must always be considered, however, as they frequently threaten one or another vital process and can cause overwhelming discomfort. Effective treatment, which is often possible, depends on accurate diagnosis, but diagnosis can be made difficult by the crowding of vital and sensitive structures into one rather small region of the body.

Nose and Sinuses

A wide variety of systemic and local processes may be reflected in symptoms referred to the nose, and trauma to the nose may have serious consequences for vision or the brain. It is an error to neglect the possible broader implications of complaints that seem confined to the nasal structures. Table 1 summarizes diagnoses that should be considered when nasal trauma, epistaxis, obstruction sinusitis, or facial pain are the presenting problem.

Trauma. After an injury, the patient should be evaluated for damage extending beyond the nose itself. Careful clinical evaluation and x-rays as appropriate will reveal significant fractures in cases that first appear to represent simple nasal injuries. More complex fractures of the facial skeleton, such as the LeFort types I, II, and III, also will be revealed.

A fracture through the cribriform plate of the ethmoid bone, which forms part of the roof of the nose, may open communication between the respiratory passage and the cerebrospinal fluid space and thus predispose to meningitis. Likewise, a fracture through the walls of the frontal or sphenoid sinuses may enter the subarachnoid space.

If the wall of the orbit is fractured, the eye may become displaced, or the eye muscles entrapped, and visual disturbances result. But symptoms may not appear until edema subsides, days or even weeks after the injury. The classical injury of this type is the "blowout" fracture in which hydrostatic pressure of the orbit's soft tissues, raised by a blow to the eye, fractures the floor of the orbit and herniates the soft tissue, including extraocular muscles, into the maxillary sinus. Complications can be prevented by timely surgery to repair the orbital floor.

A hematoma of the nasal septum left undetected can lead to collapse of the external nose as a result of

TABLE 1

NOSE AND NASAL PASSAGES, SYMPTOMS AND CRUCIAL DIAGNOSES	
Disorder	
Trauma	Cribiform plate fracture Orbital fracture Septal hematoma Le Fort fracture
Epistaxis	Hematologic disorders Intranasal or sinus neoplasm Nasopharyngeal neoplasm
Nasal Obstruction	Intranasal tumor Meningocele or encephalocele Nasal polyps in children (cystic fibrosis)
Sinusitis	Fungus Tuberculosis Neoplasm of sinus Wegener's Granulomatosis Midline granuloma
Facial Pain	Trigeminal nerve irritation by tumor Vascular facial pain

cartilage resorption; an unsightly "saddle nose" deformity ensues. This complication can be prevented by early incision and drainage of the hematoma.

Epistaxis. Whereas the vast majority of nose bleeds are due to local irritation, recurrent epistaxis may signal either a hematologic disorder or neoplasm within the nose, the nasopharynx, or a sinus. Appropriate blood tests, examination after "shrinking" the nasal mucosa with Neosynephrine®, and radiograms will aid in diagnosing the cause of nose bleeds.

Intranasal masses. Not every swelling in the nose represents a polyp. Because of the shape of the nasal chamber most masses are molded to resemble a benign polyp. Many lesions masquerade as polyps, among them benign neoplasms, malignant tumors, hemangiomas, and encephaloceles. The physician should become suspicious about "polyps" if a) the mass is unilateral, b) there is intranasal bleeding or blood-tinged mucous surrounding the mass, c) there is no past history of nasal polyps, or d) there is an associated swelling of the face or about the eye.

Polyps in children are uncommon. When bilateral they may signal the presence of cystic fibrosis; when unilateral they may represent either an intranasal encephalocele or a malignant tumor. The inadvertent biopsy or removal of an unsuspected encephalocele or meningocele may result in meningitis. Appropriate

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radiograms will reveal the nature of these masses by demonstrating a defect in the osseous roof of the nose. The mass must be removed by a neurosurgeon who will also repair the defect in the roof of the nose to prevent a recurrence of the herniation.

Sinusitis. Acute sinusitis when uncomplicated appears as nasal stuffiness and rhinorrhea accompanied by varying degrees of facial pain or headache; the chronic condition usually has even fewer symptoms, or sometimes none at all. Some nasal blockage with or without rhinorrhea and a mild discomfort over the affected sinus is not an uncommon presentation of chronic sinusitis.

When sinus symptoms are unexpectedly prolonged and resistant to the usual methods of treatment, a more serious pathologic process may be at work, such as tuberculosis, or fungal disease. A particularly serious infection of the sinuses in diabetics is caused by the fungus *mucor*, which can spread rapidly to the brain. Treatment for mucormycosis with amphotericin and surgery is not highly effective but offers the only hope of cure.

Wegener's granuloma and lethal midline granuloma are two non-infectious inflammatory disorders which often begin in the nose and sinuses; they cause a sinusitis which heralds the onset of life-threatening disease. As Wegener's granuloma evolves the sinusitis becomes destructive; the disease subsequently may become multicentric, but is likely to involve particularly the lungs and kidneys. Lethal midline granuloma believed to be a localized form of lymphoma, literally destroys the midline structures of the nose and face. Both of these diseases are now treatable with considerable success: Wegener's with cytotoxic drugs and lethal midline granuloma with radiation therapy.

Facial pain masquerading as sinusitis. The common causes of persistent facial pain—diseases of the teeth and paranasal sinuses—can easily be ruled out with appropriate x-rays. Among the remaining, more elusive causes are vascular pain and compression of the trigeminal nerve by either a neoplasm or an abnormal vascular loop.

Vascular pain of the face usually occurs in individuals with a personal or family history of migraine; its pathogenesis is unknown. The pain is most often unilateral and does not follow the distribution of any branch of the trigeminal nerve. Vascular pain differs from typical migraine in its location (face and jaws) and persistence (days or weeks), and in that it is not commonly accompanied by nausea. When the examiner carefully compresses all the palpable branches of the external carotid artery on both sides of the face, tenderness is elicited from vessels on the side of the orofacial pain. Failure to identify this condition may result in futile dental or sinus surgery. This type of orofacial pain can be relieved with Amitriptyline.

When facial pain assumes the distribution of one or more branches of the trigeminal nerve, and especially if it is accompanied by hypesthesia, a

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Tenuate®

(diethylpropion hydrochloride NF)

Tenuate Dospan®

(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma, agitated states. Patients with a history of drug abuse. Ouring or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect. Rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle, the patient should therefore be cautioned accordingly. **Drug Dependence:** Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychological dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. **Use in Pregnancy:** Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. **Use in Children:** Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: **Cardiovascular:** Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. **Central Nervous System:** Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache, rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. **Gastrointestinal:** Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. **Allergic:** Urticaria, rash, ecchymosis, erythema. **Endocrine:** Impotence, changes in libido, gynecomastia, menstrual upset. **Hematopoietic System:** Bone marrow depression, agranulocytosis, leukopenia. **Miscellaneous:** A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSEAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg tablet three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg tablet daily swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdose include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phenolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdose.

Product Information as of April, 1976

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Merrell

TABLE 2

EAR, SYMPTOMS AND CRUCIAL DIAGNOSES

Blocked Ear	Serous otitis media due to nasopharyngeal malignancy Patulous eustachian tube Endolymphatic hydrops
Ear Drainage	Chronic otitis media Carcinoma of ear canal or middle ear
Hearing Loss	Acoustic neuroma Chemodectoma
Tinnitus	Acoustic neuroma Ototoxic antibiotics
Otalgia	Referred ear pain Malignancy Malignant external otitis
Dizziness	Perilymph fistula Fistula of semicircular canal Acoustic neuroma Ototoxic antibiotics Temporal bone fracture

neoplastic irritation of the nerve must be suspected. This type of trigeminal pain may be paroxysmal, like tic douloureux, or it may be constant and severe, though not as excruciating as the pain of trigeminal tic. The nerve or one of its branches may be compressed either by an intracranial tumor or by an extracranial neoplasm, most often one that originates in the paranasal sinuses, oral cavity, or orbit. In rare instances, a primary neurogenic tumor such as a benign or malignant schwannoma may be the source of the pain. The diagnosis is made by physical evaluation and by appropriate x-rays. Depending upon the nature of the neoplasm, treatment requires surgery or radiation therapy, or both.

The Ear

The most common symptoms affecting the ear or arising in its structures include blockage, drainage, hearing loss, tinnitus, pain, and dizziness.

Blocked Ear. The physician can easily eliminate such external causes of ear blockage as wax or epithelial debris by cleaning the ear and visualizing the drumhead. Blockage of the middle ear with a serous effusion is usually due to a simple, transient closure of the eustachian tube as a consequence of upper respiratory infection, an attack of hay fever, or perhaps abrupt pressure changes during flight or diving into water. When serous otitis persists more than 1 or 2 weeks, nasopharyngeal malignancy may be obstructing the eustachian tube. Because an early malignancy will not be visible on x-rays the diagnosis is best made by careful examination of the nasopharynx.

When a patient complains of a blocked ear but the ear canal is unobstructed and the drumhead appears normal, the diagnosis is usually "blocked eustachian tube," and the disturbance is treated with oral antihistamines or decongestants, perhaps supplemented with nasal sprays. Two conditions which mimic the symptoms caused by a blocked eustachian tube and

are not responsive to decongestive medications are the patulous eustachian tube and endolymphatic hydrops.

A patulous, or continuously patent, eustachian tube usually appears during pregnancy or after a rapid large weight loss from illness or dieting; sometimes no explanation is apparent. The diagnostic features of the condition are autophony (an increased resonance of voice and breath sounds), a hollow or blocked feeling in the ear, and reproducible alleviation of these symptoms when the patient lies back. The diagnosis can be confirmed if the drumhead is observed to move synchronously with breathing through the nose. Medications used to treat a blocked eustachian tube worsen the symptoms of a patulous tube, which often disappear spontaneously as the patient regains his health.

Endolymphatic hydrops is due to Meniere's disease and less frequently to tertiary syphilis, trauma, or previous middle ear surgery. It produces symptoms of blockage and diminished hearing. The otoscopic examination is normal but the diagnosis can be verified by tests of hearing and vestibular function. When asked, the patient also reports noise intolerance, fluctuation in the hearing level, and sometimes recurrent vertigo. Medications do not help in the treatment of hydrops, and surgery is indicated only in those patients who have incapacitating vertigo.

Ear drainage. An external otitis may cause drainage which responds to a thorough cleaning and appropriate ear drops. When drainage persists, though, there may be a more serious cause.

Most commonly otorrhea, especially when it is unilateral, is due to chronic otitis media with perforation of the drumhead. To visualize the perforation, the ear canal must first be thoroughly cleaned. The defect is sometimes easily seen if it is in the pars tensa, but a small perforation may be obscured by edema of the surrounding drum. In this circumstance, negative pressure applied with a pneumatic otoscope will suck the secretions through the perforation and thus identify the defect. A perforation located in the pars flaccida is often overlooked in a cursory otoscopic examination. An untreated, chronic otitis media may be followed by such serious complications as facial paralysis, intracranial sepsis, septicemia, and labyrinthine destruction. In most patients such complications can be averted by proper diagnosis and management, which is usually surgical.

Although carcinoma of the external auditory canal and middle ear is uncommon, its initial manifestation may simply be protracted drainage. Whenever a patient with stubborn "external otitis" is found to have a localized redness or swelling in the external ear canal or within the drumhead, neoplasm should be suspected. When pain is also present, the diagnosis becomes even more probable. Untreated carcinoma of the ear canal and middle ear is lethal but caught early it may be successfully treated with surgery and radiation.

Hearing loss. Most causes of hearing impairment do not significantly threaten health. Acoustic neuroma and middle ear chemodectoma are exceptions (as are chronic otitis media and nasopharyngeal carcinoma which are discussed elsewhere in this chapter).

Unilateral tinnitus and hearing loss are the earliest symptoms of acoustic neuroma, a benign tumor and the most common neoplasm of the posterior cranial fossa. This tumor can be accurately diagnosed with appropriate audiovestibular and radiologic examinations long before the appearance of such advanced findings as papilledema, ataxia, facial paralysis, and trigeminal nerve dysfunction. Present-day microsurgical techniques make it possible to resect these tumors when they are still small (under 2 to 3 cm) and achieve an acceptably low morbidity and mortality rate. Outcome is less favorable when the tumors are diagnosed after they have begun to produce neurologic signs and symptoms such as headache, cerebellar ataxia, and dysfunction of the trigeminal nerve.

Chemodectomas are relatively rare tumors, usually benign, that arise from chemoreceptor cells of the glomus jugulare or glomus tympanicum when they affect the middle ear. The earliest symptoms include blocked ear, tinnitus, and a mild aching discomfort in the ear. These tumors enlarge progressively and erode into the inner ear, facial nerve, intracranial spaces, and finally the deep compartments at the base of the skull and upper neck. Chemodectomas may be diagnosed by physical examination and their full extent assessed by radiologic studies. In early stages, chemodectomas can be resected completely with minimal loss of function in the ear and lower cranial nerves. In advanced stages, these growths are virtually unresectable, though they may be arrested by radiation therapy. The earliest sign is often a small red or violaceous discoloration medial to the drumhead and an air fluid level due to obstruction of the eustachian tube. Compression of the vagus nerve, which emerges from the skull base beneath the middle ear, may occur and result in hoarseness due to a vocal cord paralysis.

Tinnitus. Although cochlear degeneration due to acoustic trauma, presbycusis, past otitis media, and ototoxic drugs is a more common cause of tinnitus, it must be emphasized that any patient who experiences *unilateral* tinnitus should be evaluated for the possible presence of a small acoustic neuroma.

Otalgia. Pain within the ear may result from intrinsic disorders or may be referred from any of several remote sites.

Otitis media and mastoiditis, of course, may be responsible for earache, and so may neoplasms or Wegener's granuloma arising within the ear. Wegener's granuloma may, indeed, first present as intractable otitis media and pain.

Because innervation of the ear arises from cranial nerves 5, 7, 9, and 10 and arrives by complex routes, a large number of disorders affecting relatively

remote sites can produce pain referred to the ear. Tumors and chronic inflammatory disorders in the paranasal sinuses and oral cavity including dental diseases may cause referred pain through the fifth nerve. Acoustic neuroma and herpes zoster oticus produce ear pain by way of the sensory division of the seventh nerve. Neoplasms of the tonsil and base of the tongue transmit pain to the ear through the ninth nerve, and tumors of the hypopharynx, larynx, and esophagus refer their pain through the tenth nerve. It should be apparent that the patient who complains of ear pain but has no auditory symptoms and is normal to otoscopic examination may be suffering from a serious disease in another structure of the upper respiratory or digestive systems. Such cases should not be diagnosed as "neuralgia" and should not be treated with ear drops and antibiotics for what is presumed to be an "occult" ear infection.

One form of external otitis which is characterized by persistent inflammation and severe otalgia is worthy of special mention. This is the "malignant" external otitis encountered in diabetic patients. This is a progressively spreading infection almost always due to *Pseudomonas aeruginosa*. The infection is not responsive to the treatment that is usually effective: drops, local heat, and oral antibiotics. If unchecked by intensive parenteral antibiotic treatment, it commonly progresses to an osteomyelitis of the temporal bone and may go on to intracranial sepsis.

Dizziness. Not all dizziness is due to aural disease and not all aural vertigo is of crucial importance. The most serious forms of aural vertigo include labyrinthitis associated with acute otitis media, labyrinthitis complicating chronic otitis media, tumors involving the vestibulocochlear nerve, progressive vestibular destruction by certain ototoxic antibiotics, middle ear perilymph fistula, post-stapedectomy vertigo, and vertigo after a basilar skull fracture.

Whereas the middle ear normally communicates with the nasopharynx, the inner ear is sealed off from direct communication with the upper respiratory tract. But the inner ear normally communicates with the subarachnoid space through the afferent vestibulocochlear nerve fibers and by the cochlear aqueduct. Therefore, whenever trauma or a disease process produces an abnormal communication between the middle and inner ears a pathway is established for infection to spread from the upper respiratory tract to the intracranial spaces.

When a patient with an ordinary acute otitis develops vertigo, nystagmus, and ataxia, the labyrinth is being irritated. If antibiotic therapy is not immediately instituted, the infection may spread to the inner ear. The consequence can be complete destruction of the inner ear as well as intracranial sepsis. Similarly, chronic otitis media may be complicated by labyrinthine invasion, a special form of which is the labyrinthine fistula. In this condition the chronic infection has eroded the bone surrounding the horizontal semicircular canal; only a tenuous soft tissue barrier is left between the infected middle ear and the

inner ear. At this stage the patient experiences intermittent vertigo and ataxia exacerbated by any maneuver transmitting pressure to the inner ear. The patient, for example, experiences vertigo when he places a finger in the ear canal. If this complication is recognized, the function of the ear can usually be saved by appropriate surgery. If the disease progresses unchecked, the patient may develop a suppurative labyrinthitis with irreversible destruction of the inner ear and is at risk of developing intracranial sepsis.

Tumors affecting the vestibulocochlear nerve produce vertigo as well as hearing impairment; these include acoustic neuroma and meningioma of the petrous ridge.

Hearing loss due to certain aminoglycoside antibiotics such as neomycin and kanamycin is an undesirable side effect which is familiar. Toxicity to the vestibular organs is less well recognized but may have an even more profound effect on the patient than hearing impairment. Progressive irreversible vestibular destruction can be caused by certain of the aminoglycoside antibiotics, gentamicin and streptomycin, among them, which affect the vestibular organs before hearing is affected. If the vestibular apparatus is destroyed completely, the patient may become an invalid. Patients receiving these drugs should be monitored not only for hearing but vestibular function, and if it begins to deteriorate, a different antibiotic should be seriously considered. In particular, older patients, who are already handicapped by poor muscular development and failing vision compensate poorly for any loss of vestibular function.

A perilymphatic fistula is an abnormal communication between the middle and inner ears through either the oval or the round window. It results from head injury; ear pressure changes, as in diving or flying; and sometimes normal physical exertion, as when transiently elevated pressure of the spinal fluid is transmitted via the cochlear aqueduct to the inner ear fluid, which in turn bursts one of the windows to the middle ear. A fistula should also be suspected in a patient who has had a stapedectomy and suddenly develops hearing loss and dizziness: the prosthesis may have become displaced with resultant rupture of the oval window. In this condition, the patient has a sensation of fullness and hearing loss in the affected ear and feels varying degrees of ataxia and vertigo. Not only are the ear symptoms annoying and possibly disabling, but they are also harbingers of serious complications: should the patient develop otitis media during an upper respiratory tract infection, labyrinthitis may develop.

A perilymph fistula may be surgically sealed if diagnosed in time. The procedure may succeed in preserving the function of the ear as well as rendering it safe in the event of future infections.

A patient who develops hearing loss, dizziness, and ataxia after a severe head injury may have sustained a fracture of the temporal bone with damage to or even

TABLE 3

FACIAL PARALYSIS, CRUCIAL DIAGNOSES

The diagnosis of Bell's Palsy should not be made until the following conditions have been ruled out:

1. Acoustic neuroma
2. Meningioma
3. Chemodectoma
4. Carcinoma of ear
5. Parotid malignancy
6. Sarcoid
7. Herpes zoster (Ramsay Hunt Syndrome)
8. Tympanomastoiditis

destruction of the inner ear. When the fracture is relatively small and especially when it is limited to the temporal bone, it may not appear on ordinary skull x-rays. The patient should undergo polytomograph studies of the ears in the anterior, posterior, and lateral projections. Although correctly diagnosing this injury does not permit correction of the disrupted function of the ear, it may lead to a diagnosis of spinal fluid leakage. The leak may not be evident externally, for it may enter an intact middle ear and discharge into the nasopharynx by way of the eustachian tube. If suspected, a leak can be revealed by instilling a tracer substance into the subarachnoid space with a lumbar puncture and then identifying the tracer in the nasopharynx near the orifice of the eustachian tube. Once diagnosed, the leak must be corrected surgically in order to prevent meningitis.

Facial paralysis. A common diagnostic pitfall is the assumption that a facial paralysis occurring in an otherwise healthy person is Bell's palsy. Yet the term "Bell's palsy" refers only to an idiopathic paralysis which is usually unilateral and of sudden onset. Many cases of facial paralysis are not, in fact, idiopathic but instead herald a serious disease. The facial nerve is vulnerable to injury from many processes; it exits from the brain stem, passes through the internal auditory canal and thence through a lengthy tunnel within the temporal bone, exits from the base of the skull, passes through the substance of the parotid gland and then is distributed to the muscles of facial expression. Facial paralysis may, thus, result from compression caused by a tumor in the posterior cranial fossa (usually an acoustic neuroma or meningioma), tumors of the temporal bone (especially chemodectoma and carcinoma), or a malignant tumor of the parotid gland. In addition, a facial paralysis may signal neuritis such as that caused by sarcoid, herpes zoster, acute otitis media or chronic tympanomastoiditis. The diagnosis of Bell's palsy should not be made until these more serious, and as a rule treatable, causes of facial nerve injury have been carefully excluded.

The Oral Cavity

Among pathologic processes affecting the oral cavity, the most important to diagnose early is carcinoma. Any lesion of the mucous membrane which

TABLE 4

INTRAORAL LESIONS
Carcinoma
Mucosal lesions due to hematologic disorders
Amyloidosis
Muco-ulcerative disorders (pemphigus, Behcet's disease, Stevens-Johnson Syndrome)
Tuberculosis
Syphilis
Lingual abscess
Ludwig's abscess
Ludwig's angina
Parapharyngeal abscess
Masseter space infection

fails to heal spontaneously within 2 or 3 weeks, especially in an individual with constant tobacco use or heavy alcohol intake, should be suspected of being malignant. Oral cancers may be found in any part of the oral cavity, although they are most common in the floor of the mouth and on the tongue; the surface of the lesion is usually ulcerated but may remain intact. White patches (leukoplakia) and red patches (erythroplasia) may be premalignant and should be viewed with suspicion. Intraoral lesions diagnosed early may be cured by relatively small surgical procedures or by radiation therapy. When malignancies have grown over 1 to 2 cm they have had time to allow metastases to develop.

Systemic diseases of various kinds may first produce intraoral lesions. Leukocyte and platelet disorders sometimes have their earliest manifestations in the oral mucosa, where they can cause infected ulcerations or purpuric and ecchymotic spots. Both amyloidosis, which causes thickening of the tongue, and the muco-ulcerative disorders (Behcet's disease, pemphigus, and Stevens-Johnson syndrome) also often announce themselves with oral lesions.

Systemic infections, for example tuberculosis or syphilis may begin in the mouth. Many others remain localized in the oral cavity and adjacent fascial compartments of the neck. Lingual abscess, abscess of the masseter space, parapharyngeal abscess, and Ludwig's angina, which is an infection of the floor of the mouth, though localized, are all threats to life because they can lead to obstruction of the upper airway or to septicemia. Short of that, they can cause permanent masticatory difficulty by producing fibrosis of the masticatory muscles.

Pharynx and Larynx

A neoplasm of the oropharynx should be suspected when any swelling or ulceration persists more than two weeks. Particularly likely lesions are an asymmetric swelling of a tonsil, a persistent tonsillar ulceration, or a painful lesion on the posterior or lateral walls of the oropharynx posterior to the plane of the tonsil. Malignant lesions of the oropharynx are mainly epidermoid carcinoma and lymphoma and are often accompanied by pain referred to one or both ears. Referred otalgia in association with an indolent pharyngeal lesion should always be viewed

TABLE 5

PHARYNX AND LARYNX, SERIOUS DISORDERS	
Neoplasm	— Oral cavity Nasopharynx Oropharynx Laryngopharynx
Infections	— Retropharyngeal abscess Epiglottitis Peritonsillar abscess Tuberculosis laryngitis
Chemical Burns	— Oral cavity Pharynx Larynx Esophagus

with a high degree of suspicion of malignancy.

Neoplasms of the nasopharynx are not readily seen since examining this portion of the pharynx requires facility with the use of a small mirror. They simply cannot be seen by inspecting the throat with a tongue depressor and flashlight. Nevertheless, lesions of the nasopharynx should always be suspected when one or a combination of the following signs and symptoms is present: recurrent epistaxis or pharyngeal bleeding, referred otalgia, middle ear effusion, abducens muscle palsy, an unexplained neck mass, nasal obstruction, or unexplained neurologic involvement of cranial nerves 9 to 12. These tumors include mainly epidermoid carcinoma and lymphoma and they have a propensity for invading the base of the skull and then rapid intracranial growth.

Neoplasms of the hypopharynx and larynx should be suspected when one or a combination of the following signs or symptoms persists: throat pain (with or without referred otalgia), dysphagia, odynophagia, voice change (hoarseness or a muffled voice), and enlarged lymph nodes in the neck. Hoarseness is not a necessary sign; it occurs only with the minority of laryngopharyngeal cancers—those which involve the true vocal cord or the recurrent laryngeal nerve.

As with nasopharyngeal malignancies, it must be emphasized that *laryngopharyngeal lesions can never be detected by means of a tongue depressor and flashlight, but require a mirror examination*. Furthermore, a negative radiogram of the neck and pharynx may prove misleading in seeming to "rule out" a malignant lesion. These tumors should be diagnosed when they are small and at that stage they may not be manifest on x-rays. Finally, one should not make the common misjudgement of diagnosing "laryngitis" in a patient who has persistent hoarseness, regardless of age. Laryngeal malignancies can occur in individuals of all ages.

Infections of the pharynx may seriously compromise a patient's airway, in part because the submucosa of the upper respiratory tract down to and including the larynx is loose and capable of rapid swelling. Such conditions as retropharyngeal abscess, epiglottitis, epiglottic abscess, tuberculous laryn-

TABLE 6

CAUSES OF LARYNGEAL PARALYSIS

1. Thyroid carcinoma
2. Metastatic carcinoma in jugular foramen
3. Glomus jugulare tumor
4. Laryngopharyngeal carcinoma invading the recurrent laryngeal nerve
5. Esophageal carcinoma invading the recurrent laryngeal nerve
6. Carcinoma of lung
7. Mediastinal tumor
8. Tumor in posterior cranial fossa
9. Neurofibroma of vagus nerve in the neck
10. Idiopathic

gitis, peritonsillar abscess, and relatively minor infections in a patient whose airway is already reduced by vocal-cord paralysis, tracheal stenosis, or a like condition—all these require hospitalization, intensive treatment with antibiotics, and especially careful observation until the infection is under control. Diagnosis is made by mirror examination and x-rays.

Chemical burns of the oral cavity may extend to the hypopharynx and esophagus, where they can cause rapid airway obstruction and permanent scarring, if the patient survives the acute episode. Lye is even more destructive to the mucosa and submucosa than acid. The extent of a burn can be determined only by endoscopic examination. Acute obstruction and cicatricial scarring of the esophagus may be prevented by intensive treatment with antibiotics and systemic corticosteroids.

Laryngeal paralysis. A patient with persistent hoarseness may have a benign growth on the vocal cords, a malignancy, or paralysis of one or both vocal cords. Laryngeal paralysis is associated with no discomfort, although there may be some transient aspiration of swallowed liquids for a few days after onset. The physician bears a heavy responsibility in making the diagnosis of laryngeal paralysis because, although idiopathic in many instances it may be caused by a lesion that compresses or invades either the vagus nerve or the recurrent laryngeal nerve. One need only consider the course and length of these nerves to appreciate the variety of lesions which may disturb their function: metastatic tumor of the jugular foramen, metastatic lymph nodes in the neck, thyroid carcinoma, tumors of the superior mediastinum, and bronchogenic carcinoma, among others, all located in sites relatively remote from the larynx. As is the case with all neoplasms, the earlier the disease is diagnosed the better is the hope for effective treatment.

"Sore throat" from thyroiditis. This entity deserves mention because the diagnosis is so often missed and the patient treated inappropriately. Patients with thyroiditis complain of a sore throat when they mean a sore neck. When, on superficial examination, some redness is seen in the pharynx, and the neck is somewhat tender, "pharyngitis with mild cervical lymphadenitis" is diagnosed. The patients, who usually have deQuervain's thyroiditis, are

TABLE 7

NECK MASSES, CRUCIAL DIAGNOSES

Metastases to lymph node
(primary tumor above clavicle in 75% of cases)
Lymphoma
Malignant neoplasm of tail of parotid gland
Malignant neoplasm of submandibular salivary gland
Thyroid carcinoma
Carotid body chemodectoma

treated with successive courses of antibiotics. This disorder, which may be self limited, may seem to respond to the antibiotics or may persist and the diagnosis remain obscure. In cases of "puzzling throat discomfort," if the thyroid gland is carefully palpated and found to be tender, with or without enlargement, thyroiditis is the probable cause.

Neck Masses, Neck Pain, and Neck Injury

The most threatening masses found in the neck include metastases to lymph nodes, lymphomatous nodes, tumors of the two major salivary glands (the parotid and submandibular), thyroid carcinoma, and carotid-body tumor. In the majority of patients with cervical lymph nodes enlarged by metastases, the primary tumor is located above the clavicles. Initial attention should therefore be given to the nose, pharynx, oral cavity, sinuses, salivary glands, laryngopharynx, and thyroid as the probable source. If these all prove negative, the primary tumor must be sought below the clavicle.

Even though a neck mass may be due to metastatic spread from a primary tumor, the prognosis is not hopeless. The cervical lymph nodes act as effective filters and barriers to entrap metastatic emboli for at least a few months before they escape and metastasize to sites below the clavicles. The outlook dims when a metastatic node is larger than about 3 cm, when it is located low in the neck, or when it becomes fixed to its bed (an indication that the tumor has grown through the capsule of the lymph node). Therefore, the diagnosis of possible malignancy and the location of the primary source should be promptly pursued.

Two points about the parotid salivary gland require emphasis. First, although the majority of tumors of this gland are benign, 20 to 25 percent are malignant. Second, the lower portion, or tail, of the parotid gland extends approximately to the level of the hyoid bone so that in masses located in the upper part of the neck, the differential diagnosis includes parotid tumors as well as enlarged lymph nodes. By contrast, tumors of the submandibular salivary gland are more likely to be malignant than benign.

Thyroid carcinoma should be suspected in all cases of thyroid enlargement and can be diagnosed by radionuclide scans and biopsy. The chemodectoma arising from the carotid body is a highly vascular tumor located at the bifurcation of the carotid artery.



Continued on Page 298

Blue Cross and Blue Shield Central Certification Coverage

A Guide for the Health Care Provider

Subscriber's Name —

Group Number —

		
Blue Cross and Blue Shield		EFFECTIVE DATE 8-1-79
SUBSCRIBER'S NAME JOHN Q. PUBLIC		
IDENTIFICATION CODE & NUMBER XYZ123456789		
GROUP NUMBER XYZ111	BLUE SHIELD PLAN CODE 222	BLUE CROSS PLAN CODE 111
GROUP NAME XYZ CORPORATION		

Subscriber's
Identification Number

Be sure to give your local
Blue Cross and Blue Shield Plan
these three pieces of
information!

What is "Central Certification?"

"Central certification" is a special way of covering certain Blue Cross and Blue Shield Plan subscribers. It is used for employees of a company that has plants, offices and people in several different states; whose employees often travel a great deal or change location frequently; and which has all of its personnel, payroll and health coverage records in one place.

For these companies, Blue Cross and Blue Shield Plans offer central certification.

All records are kept by one Plan, (called the "control Plan"), which is usually the Plan located in the company's headquarters city.

The control Plan issues identification cards to all employees of that company, regardless of their location.

However, a central certification subscriber is treated exactly like any subscriber of your local Blue Cross and Blue Shield Plan. You accept the central certification card just as you accept a card from your local area Plan.

The Card

The card—a sample is reproduced at the top of this guide—is distinctive. It is carried only by central certification subscribers. Along with the subscriber's name and identification number, the card also has a six-character group number that is special. The three letters identify the company the subscriber works for and the three numbers identify the Blue Cross and Blue Shield control Plan.



What You Do

When a central certification subscriber comes to you for care, treat the patient exactly as you would any other Blue Cross and Blue Shield Plan subscriber. Give your local Plan:

the name: John Q. Public
the identification number: XYZ123456789
the group number: XYZ111

The local Plan will then cover the benefits to which the subscriber is entitled.

Special Note: Report both outpatient cases and inpatient cases to your local Blue Cross and Blue Shield Plan. Most central certification subscribers have comprehensive coverage, including outpatient benefits.

After the patient is discharged, or has received outpatient services, the local Blue Cross and Blue Shield Plan will pay you just as it would for any of its local subscribers.

Please Remember . . .

Central certification is a great convenience for a company with employees scattered throughout several states.

In almost all cases, the patient lives and works in your community.

Just remember that the central certification subscriber—as far as you're concerned—is exactly the same as any local Blue Cross and Blue Shield Plan subscriber.

You deal only with your local Blue Cross and Blue Shield Plan.

You will be paid by the local Blue Cross and Blue Shield Plan.

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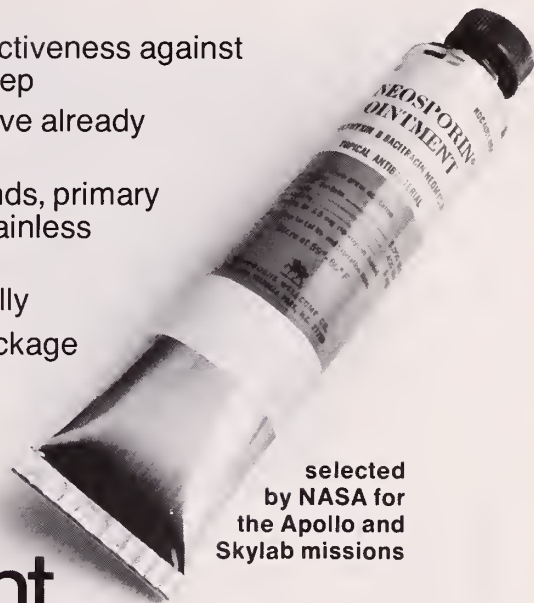
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WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as a failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

PRECAUTIONS: As with other antibacterial preparations,

prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Management of anxiety disorders, or short-term relief of symptoms of anxiety; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders, atetosis, stiff-man syndrome, convulsive disorders (not for sole therapy)

The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma. may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication, abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported, should these occur, discontinue drug. Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long-term therapy.

Letter To The Editor

To the Editor:

Re: Cimetidine for Pruritus in Hodgkin's Disease

Cimetidine, a potent histamine H₂ receptor antagonist, has been shown to be effective for the pruritus associated with polycythemia vera¹ although the mechanism for pruritus in the myeloproliferative disorders has been attributed to histamine H₁ receptors.² Another report in the Journal³ has documented similar success; but a study of cimetidine in 12 patients with polycythemia vera failed to confirm any benefit.⁴

Recently, four patients with pruritus related to Hodgkin's disease were treated with cimetidine one gram daily.⁵ The pruritus disappeared within 1-4 days after treatment was initiated and recurred within 1-10 days after the medication was discontinued. Other antipruritic agents were not uniformly used.

Three patients with Hodgkin's disease who relapsed after primary therapy and developed pruritus are presented. Each received cimetidine 300mg. t.i.d.. Only one patient responded. A 26-year-old male with III B disease (nodular sclerosis) who was initially treated with the 8 drug program (MOPP/ABDV)⁶ relapsed after one year. Pruritus and recurrent nodes developed. Prior to definitive therapy, cimetidine was given for a two-week trial after lack of response to diphenylhydramine and cyproheptadine. There was no response. A 28-year-old male with IV B disease (nodular sclerosis) relapsed after treatment with the MOPP/ABDV program. Cimetidine was given for pruritus without benefit. Diphenylhydramine was then successful in relieving his symptoms but produced excessive drowsiness even at a dose of 25mg. A 41-year-old male with IV B disease (nodular sclerosis) relapsed after initial treatment for widespread disease including bone involvement. He was treated for pruritus with diphenylhydramine without success. Cimetidine produced significant relief within 48 hours.

Continued on Page 351



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PARCOURSE Fitness Circuit Opened

In a cooperative effort to give the people of greater Portland a novel means of improving their physical fitness, Blue Cross and Blue Shield of Maine and the city of Portland have opened a PARCOURSE Fitness Circuit on Baxter Boulevard in Portland. If this project is successful, other PARCOURSES for the cities of Lewiston, Bangor and Presque Isle will also be considered.

Blue Cross and Blue Shield Plan President, George E. McLean, officially turned the PARCOURSE over to Portland's mayor, John O'Leary, in opening day ceremony held September 11th.

"PARCOURSES" originated in Switzerland and are a series of 18 outdoor exercise stations spaced over a one to two and one-half mile path. They are designed for people in all levels of physical fitness, from the beginner to the advanced athlete.

The circuit combines a wide variety of activities designed to strengthen the cardiovascular and musculo-skeletal systems of the human body. Each station in the PARCOURSE provides an exercise that helps improve flexibility, strength and muscle tone. Exercises include: stretching, jogging, jumping, and vaulting, as well as performing chin-ups, push-ups, toe touches and other calisthenics.

Approximately \$6,000 was donated by the Blue Cross and Blue Shield of Maine for equipment and signs for the program. The city of Portland has provided the site and installation, and will provide for the fitness circuit's upkeep.



Tom Guter and Dale McNelly, Provider and Professional Relations representatives for Blue Cross and Blue Shield of Maine, try out the new PARCOURSE Fitness Circuit.

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WARNINGS:

Drug dependence: Empirin with Codeine can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of this drug and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral, narcotic-containing medications. Like other narcotic-containing medications, the drug is subject to the Federal Controlled Substances Act.

Use in ambulatory patients: Empirin with Codeine may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using this drug should be cautioned accordingly.

Interaction with other central nervous system (CNS) depressants: Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics, or other CNS depressants (including alcohol) concomitantly with Empirin with Codeine may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Use in pregnancy: Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, Empirin with Codeine should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

PRECAUTIONS:

Head injury and increased intracranial pressure: The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions: The administration of Empirin with Codeine or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Allergic: Precautions should be taken in administering salicylates to persons with known allergies: patients with nasal polyps are more likely to be hypersensitive to aspirin.

Special risk patients: Empirin with Codeine should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture, peptic ulcer, or coagulation disorders.

ADVERSE REACTIONS: The most frequently observed adverse reactions to codeine include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients and some of these adverse reactions may be alleviated if the patient lies down. Other adverse reactions include euphoria, dysphoria, constipation, and pruritus.

The most frequently observed reactions to aspirin include headache, vertigo, ringing in the ears, mental confusion, drowsiness, sweating, thirst, nausea, and vomiting. Occasional patients experience gastric irritation and bleeding with aspirin. Some patients are unable to take salicylates without developing nausea and vomiting. Hypersensitivity may be manifested by a skin rash or even an anaphylactic reaction. With these exceptions, most of the side effects occur after repeated administration of large doses.

DOSAGE AND ADMINISTRATION: Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. Empirin with Codeine is given orally. The usual adult dose for Empirin with Codeine No. 2 and No. 3 is one or two tablets every four hours as required. The usual adult dose for Empirin with Codeine No. 4 is one tablet every four hours as required.

DRUG INTERACTIONS: The CNS depressant effects of Empirin with Codeine may be additive with that of other CNS depressants. See WARNINGS.



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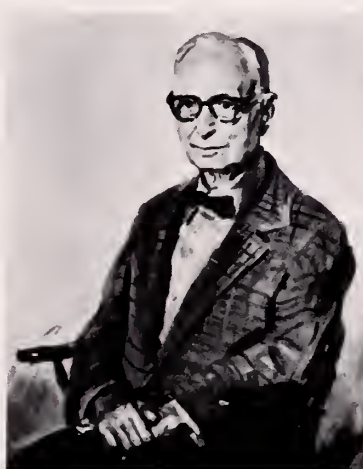
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Augusta, Maine, November 1980

Number 11

Festschrift for Isaac M. Webber, M.D.

The German term "festschrift" describes a volume of writings by several authors in tribute to a scholar or distinguished individual. This issue of *The Journal* honors Dr. Webber whose surgical progeny are among the contributors whose papers were presented at the tenth annual Maine Medical Center Surgical Symposium in March 1979. Robert M. Zollinger delivered the Isaac Webber Surgical Lecture.



Dr. Webber

Assisted by the surgical staff and Edward Churchill, M.D. of Boston, Dr. Webber initiated in 1948 the only surgical residency training program in Maine with the intent of providing the smaller communities in Maine with competent general surgeons. His legacy rests with hundreds of students and house officers who were exposed to the discipline of the teaching surgical services under his aegis. Three quarters of the surgical graduates have practiced in smaller communities in the region, raising standards of care in a tradition of excellence.

As a teacher Dr. Webber was demanding but fair and influenced his residents and colleagues by skill and example. As a surgeon he was a regional titan and, except for the early years when operating room pyrotechnics reflected his intolerance of incompetence, his performance was quietly effective, thoughtful, and gentlemanly. As a man he remains modest and totally dedicated to his profession. After more than half a century in active practice, he retired in March of 1979 but continues the habits of his distinguished career by regular attendance at departmental conferences and daily hours in the medical library. These selected papers are in the tradition of medical teaching developed at the Maine General Hospital by Isaac M. Webber.

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Percutaneous Non-operative Removal of Retained Bile Duct Stones

Up-Date 1980 A Review of 37 Patients

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ABSTRACT

Since April 1975, retained bile duct stones have been removed successfully from 31 of 34 patients using the T-Tube Tract. The 91% success rate compares favorably with the national experience. The use of large (14 fr. or more), laterally placed T-Tubes has facilitated removal. There have been no serious complications. In expert hands, ERCP has proved to be of complimentary value in one percutaneous failure and in one case of recurrent stones.

MATERIALS AND METHODS

The procedure has been described elsewhere in this journal in a previous report. All patients have had previous common duct exploration with retained stones found at the time or following surgery.

The extraction is done approximately 6 weeks after the initial surgery using the well established T-Tube tract. Multiple sessions are sometimes required. At Maine Medical Center, the extraction is considered an inpatient procedure with prearranged surgical backup.

RESULTS (SEE TABLE 1)

Of 34 patients, 10 were from Portland, 22 were from elsewhere in Maine and 2 were from New Hampshire. Thirty-one patients had successful removal of all stones. Three patients were unsuccessful.

SUCCESSFUL PATIENTS (ALL STONES REMOVED)

Of the 31 successful patients, 24 had solitary stones and 7 had multiple stones. Twenty-six had stones free in the common duct. One stone was impacted in the distal common duct. Three patients had left hepatic duct stones. One stone was located in a cystic duct remnant.

Twelve patients had stones recovered intact. One patient had a solitary stone pushed into the duodenum and recovered in the feces. Eighteen patients had stones fragmented and fragments were extracted or passed.

UNSUCCESSFUL PATIENTS

Three patients, of whom 2 had multiple stones, were unsuccessful. All 3 patients had smaller than desirable T-Tubes.

Patient #10 had 3 stones in the left hepatic duct

and the 12 french T-Tube was placed at the medial end of the incision producing a very tortuous sinus tract. Although the common duct could be entered, all control of the steerable catheter was lost due to the 360 degree bend in the tract and the 3 stones in the left hepatic duct could not be engaged.

Patient #13 also had a 12 french T-Tube and stones in the right hepatic duct and common duct. The upper stone was removed intact but forceful extraction injured the sinus tract and the tube could not be replaced.

Patient #28 was manipulated on 2 separate days. On day 1, the solitary common duct stone was encountered and crushed but not removed. The 10 french sinus tract was also dilated. On day 2 after removing a temporary tube, the sinus tract could not be renegotiated.

Subsequently, the stone was entirely removed by ERCP papillotomy.

COMPLICATIONS

Patient #8 and Patient #13 (see above) had injuries to their sinus tracts during forceful extraction of large stones.

Patient #8 was asymptomatic and required no further treatment as her solitary stone was removed.

Patient #13 developed cholangitis and the sinus tract injury prevented tube replacement. She underwent re-exploration of the duct 6-8 weeks following the procedure with removal of the remaining stone and a Roux-y choledochojejunostomy. She was well six months following her second operation.

Several patients have experienced mild febrile episodes following manipulation. All patients are routinely given broad spectrum antibiotics.

FOLLOW-UP

Patient #5 had a successful stone removal but presented with multiple recurrent stones one year later.

Patient #10, although unsuccessful, has been asymptomatic with three stones remaining in the left hepatic duct. A temporary tube left in the common duct following the attempted extraction fell out after several days.

Patient #20 returned in less than one year following complete removal of a solitary stone with multiple large recurrent stones.

These large recurrent stones were completely removed by ERCP papillotomy.

Other patients reported no further symptoms re-

Table 1

RESULTS

NO.	PATIENT	REFERRAL AREA & DATE OF REMOVAL	SEX	AGE	SIZE & NUMBER OF STONES	LOCATION	RESULTS
1	D.P.	Northern Me. 4/17/75	F	39	9 mm.	Common Duct	Removed 2. Presented as emergency with tube out.
2	S.N.	Portland 5/14/75	F	19	12 mm.	L. Hepatic Duct	Removed
3	A.M.	Southern Me. 9/12/75	F	38	* 11 mm. * 13 mm.	Both in Common Duct	Removed
4	R.B.	Portland 2/13/76	F	56	14 mm.	Impacted Distal Common Duct	Removed. 2 sessions required.
5	L.T.	Portland 8/25/76	F	74	10 mm.	Common Duct	Stone fragmented. Fragments pushed into duodenum. 2 sessions.
6	M.B.	Mid-Maine 10/8/76	F	31	8 mm.	Common Duct	Removed
7	H.W.	Mid-Maine 10/24/76	F	68	4 mm. 5 mm.	Both in Left Hepatic Duct	Removed
8	D.S.	Portland 11/22/76	F	43	15 mm.	Common Duct	Removed
9	L.R.	Portland 1/24/77	M	67	9 mm.	Common Duct	Stone removed. Half fragment removed. Other small fragments pushed into duodenum.
10	N.C.	Northern Me. 2/28/77	F	33	9 mm. 10 mm. 13 mm	L. Hepatic Duct	Unsuccessful
11	D.M.	Northern Me. 8/9/77	F	34	8 mm.	L. Hepatic Duct	Fragmented and removed
12	D.M.	Southern Me. 1/25/78	F	22	7 mm.	Common Duct	Stone pushed through ampulla of Vater into duodenum and recovered in feces within 12 hours.
13.	R.H.	Northern Me. 9/26/78	F	42	12 mm. 10 mm. ? 9 mm.	Common duct (R) Hepatic duct ? Common duct	Unsuccessful. (R) Hepatic duct stone removed, but forceful extraction injured the T-tube tract, preventing reinserion of tube.
14.	E.R.	Mid-Maine 11/13/78	M	77	10 mm.	Common duct	Fragmented and removed fragments and pushed fragments into duodenum.
15.	V.P.	Mid-Maine 11/15/78	F	90	12 mm. 12 mm. 10 mm.	Common duct	Fragmented and removed fragments in multiple sessions.
16.	J.M.	Portland 11/27/78	F	61	8 mm.	Common duct	Removed.
17.	K.W.	Portland 1/15/79	F	76	14 mm.	Common duct	Fragmented and removed.
18.	D.D.	Portland 1/29/79	F	20	6 mm.	Cystic Duct Remnant	Encountered with steerable catheter and guidewire & attempt made to fragment. Stone gone in 1 week.
19.	L.C.	Mid-Maine 2/14/79	M	66	9 mm.	Common Duct	Removed.
20.	S.E.	2/15/79	F	80	12 mm.	Common Duct	Fragmented and removed. Multiple sessions.
21.	R.N.	Northern Me. 5/10/79	M	45	7 mm.	Common Duct	Removed in two fragments.

RESULTS

NO.	PATIENT	REFERRAL AREA & DATE OF REMOVAL	SEX	AGE	SIZE & NUMBER OF STONES	LOCATION	RESULTS
22.	J.T.	Southern Maine 5/21/79	M	53	4 mm.	Common Duct	Fragments removed by suction and basket in two sessions.
23.	F.W.	Mid-Maine 6/12/79	M	73	1½ cm.	Common Duct	Fragmented and removed by basket and suction in 3 sessions.
24.	C.P.	Mid-Maine 6/14/79	M	36	8 mm.	Common Duct	Fragmented and removed by basket and suction in 2 sessions.
25.	J.M.	Mid-Maine 7/17/79	M	58	1 cm.	Common Duct	Fragmented and removed.
26.	R.S.	So. Maine 7/31/79	M	68	Several tiny fragments less than 2 mm.	Common Duct	Removed by suction and passage of instruments into duodenum.
27.	F.D.	Mid-Maine 11/2/79	M	72	12 mm. 6 mm.	Common Duct	Fragmented and removed with basket and suction.
28.	L.B.	Mid-Maine 12/11/79	F	73	10 mm.	Common Duct	Unsuccessful but stone removed by ERCP Papillotomy
29.	M.P.	Mid-Maine 12/28/79	F	70	10 mm.	Common Duct	Fragmented and removed in multiple sessions.
30.	E.L.	Portland 3/12/80	M	74	9 mm.	Common Duct	Fragmented and removed in multiple sessions
31.	G.S.	N.H. 4/2, 4/3, & 4/4/80	F	45	5 - 5-10 mm.	Common Duct	Fragmented and removed in multiple sessions.
32.	F.S.	Mid-Maine 4/14/80	F	39	1 - 8 mm.	Common Duct	Removed intact
33.	J.B.	N.H. 6/14/80	F	35	3 - 10 mm.	Common Duct	All removed intact
34.	S.S.	So. Me. 6/30/80	F	49	5 - 12 mm.	Common Duct	All removed intact

lated to the hepatobiliary system, with the exception of patient #13 who underwent re-exploration (see above).

Since June 1980, 3 additional patients with solitary common duct stones have been treated successfully making the results to date 34 successes, 3 failures.

ACKNOWLEDGEMENT

The author wishes to thank Dr. Douglas Howell for his skillful and successful ERCP treatment of Patients #20 and #28. Patient #28, although counted as a percutaneous failure, was nonetheless saved an unnecessary operation by using a different non-operative

approach.

The author also wishes especially to thank Drs. R.E. McAfee, R.C. Dillihunt, G.F. Sager, F.S. Ray, and W.S. MacLaughlin for their willing surgical backup support for those patients from outside the Portland area; to Patricia Norton, Eleanor Watson and Dale McLellan for their technical support; and Dr. R.G. Ware for his constant criticism.

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Maine Society of the History of Medicine Saturday, November 8, 1980—2:00 p.m.

Pen Bay Physicians Building
Pen Bay Medical Center
Rockland, Maine

Speaker: Dr. Irving A. Beck, Past President, American Osler Society; Lecturer in Medical Science, Brown University School of Medicine
Topic: "Osler's Providential Visits"
AND: Dr. Richard Kahn, President, Maine Society of the History

of Medicine
Topic: "Photographic Images of Medicine 1880-1930"
Following meeting: Buffet dinner honoring Dr. Beck at the home of Dr. Kahn in South Union.

Ultrasound and Jaundice

ANTHONY F. SALVO, M.D.*

The differential diagnosis of jaundice is frequently a challenging problem for the clinician. Diagnostic Radiology and Diagnostic Ultrasound have, in recent years, proven very helpful in this difficult problem. The traditional question is one of differentiating between a medical cause for jaundice, such as hepatitis, cirrhosis, or drug induced jaundice, and a surgical cause, such as a stricture of a major bile duct, cholelithiasis, or pancreatic carcinoma. A confusing clinical presentation is much more common than the straightforward one.

The list of radiographic procedures which has been used in the differential diagnosis of jaundice is quite extensive. An ideal study would be non-invasive, safe, and quickly performed; and it would be sensitive and accurate. Before resorting to more invasive procedures, the diagnostician should consider an ultrasound study of the liver and biliary system. Routine plain films of the abdomen, and barium studies of the gastrointestinal tract have not been sensitive indicators of obstructive jaundice. The intravenous cholangiogram is not a useful procedure if the serum bilirubin is elevated, since the likelihood of visualizing the biliary system is quite low. Radionuclide scanning is helpful in demonstrating focal liver abnormalities, but less helpful in the diagnosis of obstructive jaundice. Percutaneous transhepatic cholangiography and endoscopic retrograde cholangiopancreatography are more invasive procedures which should be delayed until later in the diagnostic evaluation of the patient. Computerized tomography has also been helpful in the study of the jaundiced patient, but the value of this study is quite dependent upon the technology of the equipment present in any individual institution.

The liver, by ultrasound, has a rather homogeneous speckled echogenic pattern throughout the parenchyma. The vascular structures such as hepatic veins and the branches of the portal vein are clearly identified as sonolucent circles or tubes within the liver. Within the liver, the normal biliary duct branches are below the threshold of resolution. When dilated, they become visible. The vascular landmarks in the region of the liver hilum which are useful in the ultrasound evaluation include the inferior vena cava, the superior mesenteric vein, the splenic vein, and the portal vein. The superior mesenteric vein joins the splenic vein to form the portal, which courses superiorly and toward the right into the liver hilum. The portal vein lies just anterior to the inferior vena cava. In some cases, it approximates it so closely that they appear, by ultrasound, to have a common wall (See Fig. 1B). The portal vein divides

into a major right and left branch. The right branch arises in a horizontal direction and goes directly toward the right side, laterally through the liver. The left portal vein comes off anteriorly and superiorly, in a very dependable branching pattern (See Fig. 1A). At this point of branching, the common hepatic or common bile duct will lie just anterior to the portal vein. It is in this area that the duct can be visualized sonographically. As the common bile duct descends toward the head of the pancreas, it will travel toward the right side of the portal vein, and then posterior, becoming imbedded in the postero-right lateral side of the pancreatic head (See Fig. 1 and 2).

The criteria used in Diagnostic Ultrasound for the demonstration of dilated intrahepatic ducts has been reported in the literature by Laing and Filly.¹ The five criteria they describe are (1) alteration in the anatomic pattern adjacent to the main right portal vein segment and the main portal vein bifurcation; (2) irregular and tortuous tubular structures in the liver hilum; (3) stellate confluence of dilated ducts; (4) acoustic enhancement behind the bile ducts; and (5) dilatation of the biliary ducts out to the periphery of the liver. The most common of these findings and the most reliable was the alteration in the anatomic pattern adjacent to the main branching point into the right and left portal veins. Irregular tortuous walls and stellate confluence of dilated ducts were the next most reliable signs of intrahepatic biliary duct dilatation (See Fig. 3 and 4).

Until recently, most of the reports concerning ultrasound and its usefulness in jaundice have centered around the diagnosis of intrahepatic biliary duct dilatation, and the criteria used for that diagnosis.²⁻⁸ More recent work by Conrad,⁹ Weill,¹⁰ and Sample¹¹ have centered upon the extrahepatic portion of the biliary duct system. In most cases, with diligent technique, the common bile duct can be identified. If the common bile duct is less than 6 mm. in diameter in a patient who has not had a cholecystectomy, it should be considered normal. Most patients with a surgical cause for jaundice will have a dilated common bile duct with a diameter greater than 8 mm. An equivocal zone exists between 6 and 8 mm.¹¹ Several investigators have also reported a "parallel channel" or "shotgun sign" which represents a dilated common bile duct coursing adjacent to the portal vein^{9,10} (See Fig. 5). The assessment of the caliber of the biliary ducts is a safe and simple procedure by ultrasound. Many larger studies have also demonstrated its accuracy.²⁻⁸ The interpretation depends a great deal on the experience of the physician. Taylor, et al have shown that the accuracy will vary from 73% after only a few weeks in interpreting the ultrasound studies, up to a rate of approximately 90% with experience.¹²

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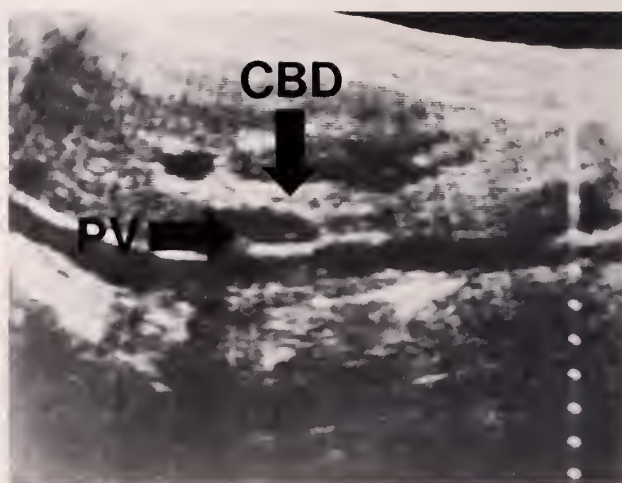


Fig. 1A and 1B. Longitudinal scans demonstrating normal portal vein anatomy. The head of the patient is at the reader's left and the feet at the reader's right. A: A longitudinal scan to the right of the midline showing the main portal vein bifurcation, with the left branch extending superiorly and anteriorly. The common bile duct is barely visible as a thin slit just anterior to the portal vein. B: A longitudinal scan closer to the midline showing the inferior vena cava behind the portal vein. The left branch of the portal vein is seen as a separate tubular structure, cut in cross-section. The common bile duct is a thin sonolucent structure just anterior to the portal vein.

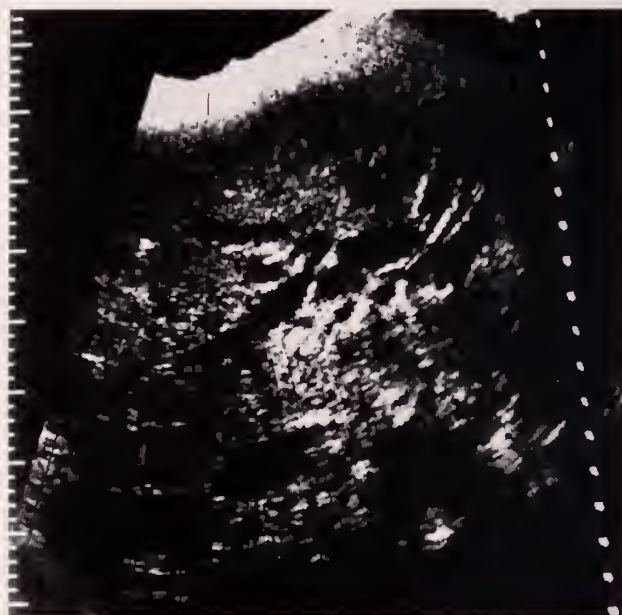
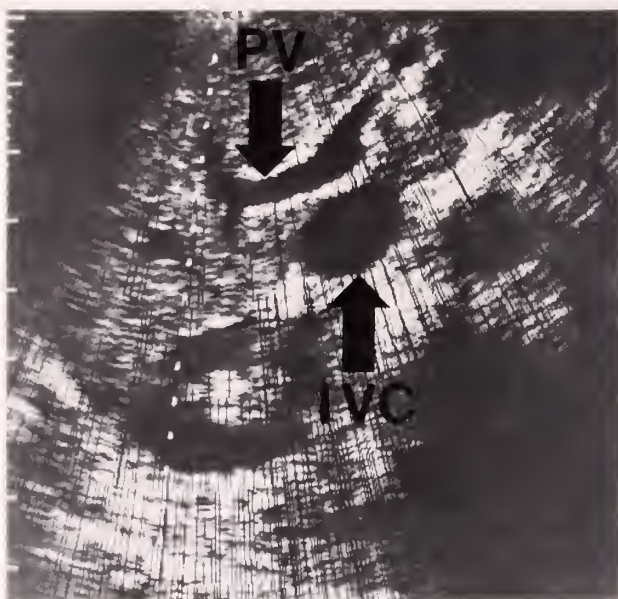


Fig. 2. An oblique scan along the longitudinal axis of the portal vein. The division of the portal vein is seen with left branch extending anteriorly. The right kidney is seen to the right and posterior to the inferior vena cava. The aorta is to the left of the inferior vena cava, just anterior to the spine.

Fig. 3. An oblique section through the liver hilum. The multiple irregular tubular and tortuous structures are dilated bile ducts, showing the distortion in the normal anatomic pattern about the liver hilum.

A review of the Maine Medical Center records of patients who were examined by both ultrasound and percutaneous transhepatic cholangiography was carried out.

The review encompassed a two-year period from January 1977 to January 1979. Thirty patients were examined by both procedures (see Table 1). Sonography identified correctly all sixteen patients with normal bile ducts, and identified twelve of the fourteen patients who were later shown by percutaneous transhepatic cholangiography to have dilated ducts. Percutaneous transhepatic cholangiography iden-

tified nine normal biliary duct systems and the fourteen dilated systems. There were seven unsuccessful percutaneous transhepatic cholangiograms, presumably in patients with normal-sized ducts. Early in our experience, no more than five or six passes were made with a skinny needle, as recommended in the literature at that time.^{13,14} Since that time, several authors have made more aggressive recommendations and more passes with the needle are being carried out in order to obtain a successful examination.

Several of the larger studies in the literature, reporting on the assessment of biliary duct caliber,

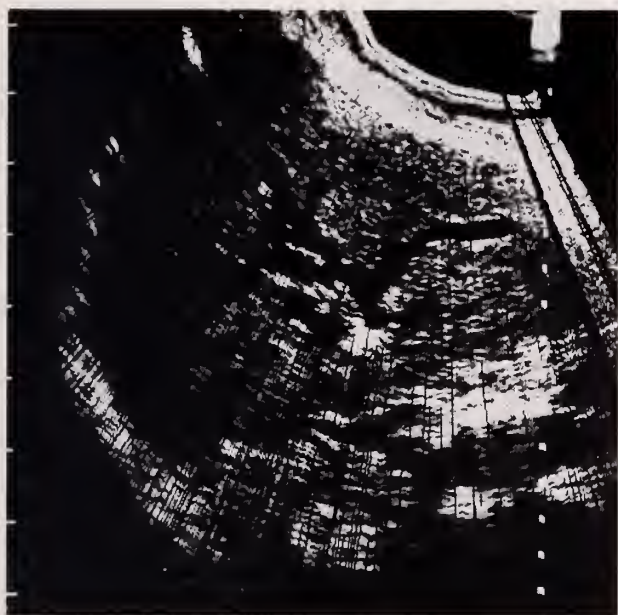


Fig. 4. A parasagittal section through the right lobe of the liver. There are tortuous and dilated bile ducts which extend out into the periphery of the liver substance.



Fig. 5. A limited sector scan along the longitudinal axis of the portal vein and common bile duct. The common bile duct is dilated, demonstrating the "parallel channel" sign. In this patient, it measures approximately 1 cm. in diameter.

have published accuracy rates ranging from 86% to 97%.²⁻⁸ In one of the larger series, Taylor, et al have reported describing the specific etiology of the biliary duct obstruction in approximately 55% of the cases by ultrasound alone.² The overall accuracy rate in these studies is consistently high (see Table 2). Medical Center survey reports an overall accuracy rate of 93% (28/30 patients).

Ultrasound should play an early role in the diagnostic evaluation of the jaundiced patient. If there is a question of obstructive jaundice, Ultra-

TABLE 1

MMC EXPERIENCE
BOTH P.T.C. + ULTRASOUND
JAN. 1977—JAN. 1979

Total 30 Pts.		
	Ultrasound	P.T.C.
Normal	18	9
Dilated	12	14

*unsuccessful P.T.C.

TABLE 2

ULTRASONOGRAPHIC ASSESSMENT OF BILE DUCTS

Date	Name	Journal	No. of Pts.	Accuracy %
1977	Taylor	Arch. Surg.	150	97%
			(Specific etiology 54.7%)	
1977	Neiman	A.J.R.	30	86%
1977	Isikoff	J.A.M.A.	40	95%
1977	Goldstein	J.A.M.A.	35	94%
1977	Vicary	Gut	24	95%
1977	Malini	Radiology	35	86%
1977	Cooperberg	J. Canad. Radiol.	47	89%
1978	Maine Medical Center		30	93%
1978	Conrad	A.J.R.	86	96%
1978	Sample	Radiology	143	91%

sound or Computerized Tomography may be used, depending upon the capabilities of the individual hospital and the technical limitations of the Computerized Scanner. If dilated ducts are discovered by Ultrasound, a specific diagnosis may be made immediately (approximately 50% of the time). Percutaneous transhepatic cholangiography or en-

doscopic retrograde cholangiopancreatography may be used as secondary studies to provide a more definitive diagnosis.

If the ducts are shown to be normal by Ultrasound, several avenues of further evaluation are open. Depending upon the individual clinical situation, conservative therapy may be undertaken. If there is

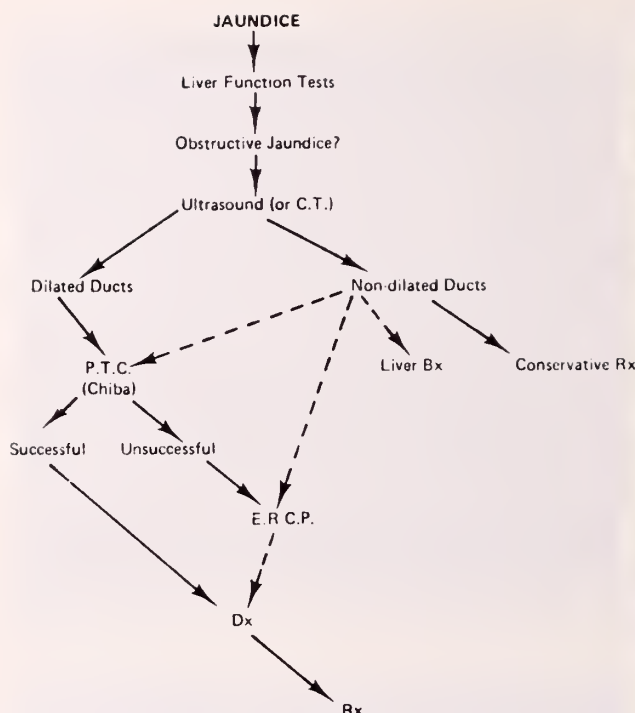


Fig. 6. An algorithm used as a guideline during the progressive evaluation of a patient with jaundice.

still a strong need to determine a specific etiologic diagnosis of the jaundice, a liver biopsy, percutaneous transhepatic cholangiography, or E.R.C.P. may still be undertaken. The Sonogram may discover metastatic disease, a liver tumor, or signs of cirrhosis, thus obviating the need for more invasive studies. It is obvious that such algorithms as shown in Figure 6 are merely suggestions which are useful in individual institutions, to be used as guides. The individual circumstances will dictate the precise studies to be used in the evaluation and the order in which they might be carried out. As well as being helpful in the diagnosis of jaundice, Radiology has also played a part, in more recent years, in the treatment for obstructive jaundice. Percutaneous biliary duct drainage has been useful as a palliative maneuver in patients who are inoperable and as a preoperative method of decompression so that the morbidity of the surgery can be lessened.¹⁵⁻¹⁷ The technique used is one involving percutaneous transhepatic cholangiography with a skinny needle to outline the duct system. Once the duct system is opacified, a sheathed needle can be placed in one of the major branches, followed by a guidewire, over which a catheter might be advanced. The catheter is positioned with side holes proximal to and distal to the point of obstruction, thus acting as a stent for biliary drainage internally, into the duodenum (See Fig. 7).

Thus, Ultrasound is considered a safe, efficient, and easily performed study and should be used early in the diagnostic evaluation of the patient with suspected obstructive jaundice.^{2,11,18,19} It can be helpful in making a specific diagnosis in more than 50% of cases. The more invasive procedures which

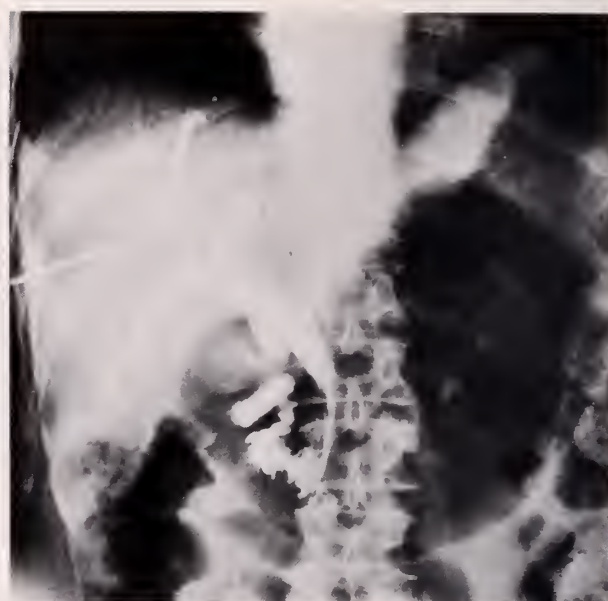


Fig. 7. A radiograph performed after percutaneous placement of a biliary drainage catheter. The common bile duct and several intrahepatic radicles are dilated and filled with contrast material. The catheter, placed percutaneously, traverses liver substance, courses through the common bile duct and into the duodenum. There are side holes above the obstruction (caused by pancreatic carcinoma) and below the obstruction in the duodenum.

opacify the biliary duct system may be used as secondary steps to outline a more specific etiology. Algorithms can be drafted, but should be used as guides, adjusted by the individual circumstances and the individual patient. Finally, diagnostic radiology may also play a part in palliation or preoperative decompression of the obstructed biliary duct system.

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Anal Fissure: A Preferred Method of Treatment

WINTHROP J. MACLAUGHLIN, JR., M.D.*

Anal fissure is one of the most common entities seen by the internist, the general practitioner, and the surgeon. This common anorectal malady causes symptoms out of proportion to its physical size, and affects individuals in all age groups. It occurs in both males and females with about equal frequency and most commonly occurs as a midlife phenomenon. The fissure usually overlies the internal and sphincter muscle somewhere between the anal verge and the dentate line, and because of its intimate association with this muscle, a brief review of the pertinent anatomy is indicated.

Extending from the termination of the ileum, the large intestine consisting of the cecum, colon, rectum and anal canal averages approximately 135 cm. in length. The muscular coats of the colon are the inner circular coat and an outer longitudinal muscular coat consisting of three narrow bands or taenia coli. Eventually the taenia coalesce to provide a complete outer longitudinal muscular coat in the rectum and the anal canal. This outer muscular coat and inner circular coat are non-striated muscle and involuntarily innervated through the sacral autonomic nerves. The parasympathetic nervous system supplies motor innervation to the internal sphincter and the sympathetic nervous system inhibits the internal sphincter muscle. Normally the internal sphincter is in a contracted state but fecal or gaseous material in the rectum will cause rectal distention and relaxation of the internal sphincter mechanism permitting evacuation of rectal contents. The outer longitudinal muscle separates the involuntary musculature of anal canal from the outer striated voluntary muscular coats. The outer voluntary muscle is normally in a relaxed state but can be contracted when there is a sensation of distention felt in the upper rectum. A more complete description of the anatomy of the rectum and anus may be found in a standard surgical text.

Patients with anal fissures generally complain of painful defecation and rectal bleeding. The pain associated with bowel movements may be described as stabbing or tearing and may persist for several hours after a bowel movement as a vague or gnawing discomfort in the anal region. Some patients state that the discomfort experienced after a bowel movement is similar to that as may be obtained from sitting on a piece of glass. Bleeding associated with these painful bowel movements is generally small in quantity and is usually only seen when a patient wipes himself and blood is noted on the toilet paper. In addition to these symptoms, the patients may also

complain of swelling, discharge, pruritis, or constipation.

Physical examination of a patient with anorectal disease is accomplished best with the patient in the jackknife position. Simple spreading the buttocks should enable the examiner to see the fissure which is generally located in the lower most portion of the anal canal. Acute fissures generally have an erythematous bed and the circular muscle fibers of the internal sphincter are not visible. More chronic fissures generally have internal sphincter fibers visible in the fissure base and are accompanied by both a sentinel skin tag located at the most distal extent and a hypertrophied papilla which is usually located just proximal to the fissure. Idiopathic fissures are generally located at the most distal extent and a hypertrophied papilla which is usually located just proximal to the fissure. Idiopathic fissures are generally located in the posterior midline but may be located anywhere about the anus. Anterior fissures are more common in female patients and are thought to be related to trauma from childbirth. Digital examination of the anal canal in patients with anal fissures may not be possible as there is usually associated marked pain and spasm which prevents introduction of the examining finger. Endoscopy should be attempted but may not be possible due to the marked spasm and resultant discomfort.

The differential diagnosis of fissures includes idiopathic fissures which are the most common, neoplastic, syphilitic, fissures secondary to inflammatory bowel disease, pruritis ani, tuberculosis and intersphincteric abscess.

The treatment of anal fissures may be divided into conservative medical treatment and surgical therapy. Conservative medical treatment is useful for fissures associated with a relatively short history. This generally consists of the use of locally applied anesthetic-containing creams, an orally ingested stool softener, and a bulk laxative. The majority of fissures will heal with this regimen within a two to three-week period. For those fissures that do not heal within this period and which are resistant to medical therapy there are a variety of surgical treatments available. The operative modalities available have ranged from sphincter stretching, fissurectomy, and posterior sphincterotomy to lateral subcutaneous internal anal sphincterotomy. The latter treatment of fissure-in-ano has become the treatment of choice in the last few years. It may be performed under local, regional, or general anesthesia and its main advantage is that it avoids an intra-anal wound, provides healing of the fissure in most cases, and affords

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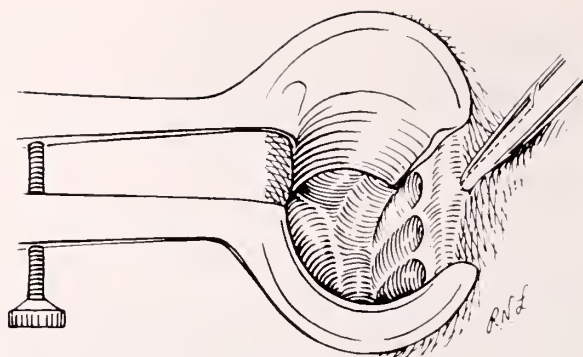


Diagram #1

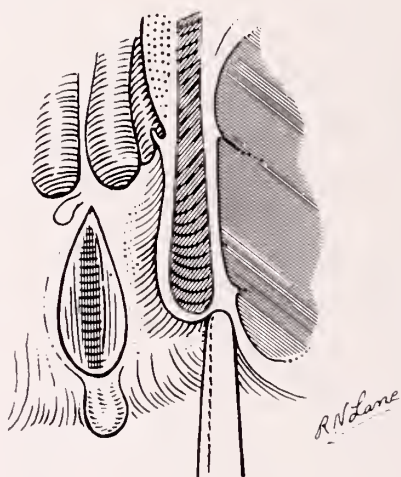


Diagram #2

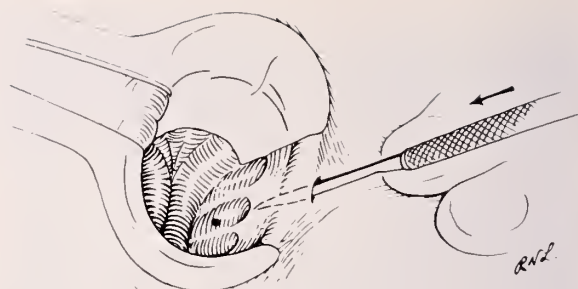


Diagram #3

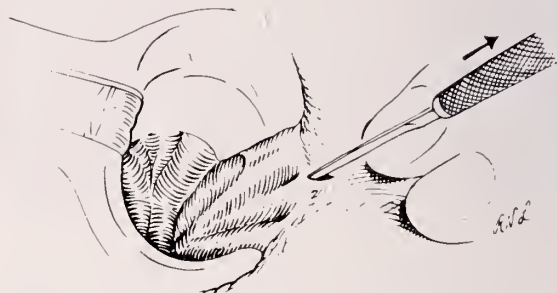


Diagram #4

almost immediate relief of symptoms. This technique was popularized by M.J. Notares,¹ and it is with his permission that the following photographs are used:

Diagram #1 demonstrates a bivalve speculum in the anal canal placing the sphincters on slight stretch. A tip of the hemostat is placed in the intersphincteric groove and the internal and sphincter muscle is visible just above it. This is best seen in Diagram #2. Diagram #3 indicates a scalpel being placed just superficial to the internal anal sphincter muscle and up to the dentate line. This is inserted parallel to it and is turned perpendicular to the internal sphincter muscle. The scalpel is then withdrawn and the internal sphincter muscle is transected as represented in Diagram #4. Hemostasis is obtained with blunt pressure. The hypertrophied papilla and sentinel skin tag may be removed if they are enlarged. A biopsy of the fissure is always done to rule out malignancy, but the fissure itself is left undisturbed and generally heals within a two to three-week period.

This operation is well accepted by patients and approximately 90% of them are satisfied with the results. There is less impairment of control of gas or

stool using the lateral subcutaneous internal sphincterotomy as compared to the open posterior internal sphincterotomy and sphincter stretching. Postoperative complications are rare but do include hemorrhage and fistula formation. Failure of the fissure to heal occurs rarely but when it does, the sphincterotomy may be repeated on the opposite side.

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Cystosarcoma Phyllodes

ALLEN F. BROWNE, M.D.* AND GEORGE F. SAGER, M.D.*

In the past 23 years, there have been ten cases of cystosarcoma phyllodes at the Maine Medical Center and Mercy Hospital (Table 1). They have all been in white females. Their ages range from 30 to 81 years with an average of 54 years. Three (33%) cases developed recurrences, one (10%) developed metastases, and two (20%) had the concurrent diagnosis of infiltrating duct cell carcinoma.

Treatment varied and included simple mastectomy, simple mastectomy followed by axillary node dissection with radiation, modified radical mastectomy, modified radical mastectomy with radiation, and wide local excision.

CASE REPORT

VC was a 35-year-old female who was found to have a 4x4x4 cm mass in her right breast while six months pregnant. Excisional biopsy was performed and showed "pericanalicular fibroadenoma." She had no other lesions or problems at that time. It was her first pregnancy, she had been on birth control pills some years before, and she was on no medication at this time.

One year later she developed another mass in her right breast and underwent bilateral subcutaneous mastectomies and silicone implants. The pathology report this time was "cystosarcoma phyllodes—malignant." The microscopic section showed a fibroepithelial tumor with hypercellularity of the stroma and frequent mitotic figures. She still showed no evidence of disease elsewhere.

Two years later, she developed a 2x3 mass on her right chest wall adjacent to her breast prosthesis. Incisional biopsy was done and then a wide local excision with another silicone reimplantation. A portion of the pectoralis major muscle was resected to obtain a margin around the tumor. The pathology report on both these specimens was cystosarcoma phyllodes—malignant. The microscopic section showed more spindle shaped cells, more hypercellularity, less ductal elements, and more mitotic figures. She still showed no evidence of disease or problem elsewhere and remains well one year later.

DISCUSSION

Cystosarcoma Phyllodes accounts for 0.5% of all malignant breast lesions and about 1% of fibroadenomatous tumors. The etiology is unclear. Some come from fibroadenomas and some arise de novo. The male cases reported in the literature^{14,16} both had gynecomastia and thus mammary alveoli which are considered to be necessary for the development of this tumor. There are no cases reported in normal prepubertal or normal male breasts.

The tumor is grouped with the other breast sarcomas by Gallager.¹² It accounts for 60% of the breast sarcomas and has a much better prognosis than the others. In the past, it has been confused with giant fibroadenoma and juvenile hypertrophy. It is

distinguished from juvenile hypertrophy because of its stromal hypercellularity. Juvenile hypertrophy is not usually unilateral and is not a tumor mass in normal breast tissue.

A patient with cystosarcoma phyllodes could be characterized as a middle-aged white female who is nulliparous and has a rapidly growing mass in one breast. The average age of occurrence is 43. It also occurs in adolescents and the elderly, however. There are two well-documented cases in males.^{14,16} It is much more common in Caucasians—4 to 1. It is more frequent in the nulliparous and a history of a rapid growth can be obtained in approximately 40% of the cases. Often a small mass has been present for years, and then it begins to grow rapidly.

Characteristically, it is a single mobile rounded or lobulated mass. Although it is notorious for its large size and one is reported at 40 cm and 8½ kg, they can be less than 2 cm. Skin changes include dilated veins and later some thinning or even pressure necrosis. Axillary adenopathy is frequent but this is very rarely tumor involvement and is usually reactive hyperplasia.

When Johannes Muller described this tumor in 1838, he used the German word "Sarkon" for the flesh-like nature of the tumor. This term did not connote malignancy until many years later. "Cysto" and "phyllodes" refer to the two other gross characteristics—cystic degeneration and leaf-like projections. The malignant potential of the tumor was not appreciated until the first collected series in 1931¹⁰ which include some microscopic changes of malignancy. The metastatic potential was not appreciated until a paper by White in 1940.¹⁹

Mammography cannot differentiate cystosarcoma phyllodes from a fibroadenoma but should be done to check for concurrent lesions. At surgery, they appear to be sharply marginated but this is actually a pseudocapsule. On microscopic exam, the epithelium of the ductal elements is normal, hyperplastic, or sometimes frankly malignant. However, there has never been a reported case of metastatic epithelial elements. The metastases are always of stromal elements. The stroma always has the characteristic hypercellularity. It may also have pleomorphism, frequent mitosis, and elements of other sarcomas such as osteogenic, liposarcoma, chondrosarcoma, fibrosarcoma, rhabdomyosarcoma, or a combination of the above.

Overall, there is about a 20-30% recurrence rate. Haagenson feels this is from inadequate local excision violating some of the bosselations beyond the pseudocapsula. The recurrences usually occur in 2-3 years but they have been reported as long as 17 years later. There is one report of a case with 14 recurrences.

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TABLE I

CYSTOSARCOMA AT MMC AND MERCY HOSPITAL FROM 1955-1978

Pt	Age	Treatment	Recurrences	Metastasis	Follow-up
EW	51	mod rad mast	no	no	10 yrs. A & W
MG	63	mod rad mast radiation	yes 5 mths	no	7 mths—death from other causes
VC	35	simple mast	yes—2 yrs.	no	2½ yrs—A & W
BB	61	mod rad mast	yes, 1 yr, 2 yrs.	yes, pulm.	3 yrs—post-op pulm. resection
GT	81	none	no	no	8 yrs—death from other causes
RP	49	simp mast. axillary diss. radiation	no	no	2 yrs—A & W
MM	60	simp mast radiation	no	no	4 yrs—A & W
LA	30	wide local excision	no	no	1 yr—A & W
HW	53	simple mast	no	no	5 yrs—death from other causes
MC	67	mod rad mast	no	no	15 yrs—A & W

Malignancy occurs in 5-10% of cases and has to be defined as metastatic disease. Some of these occur after many recurrences of what began as a benign appearing lesion and then developed some microscopic characteristics of malignancy. The question of the characteristics of benign versus malignant has been widely debated. No single characteristic is reliable. The most reliable criteria are those of Norris and Taylor and include size greater than 4 cm; greater than 3 mitosis per high power field, infiltrating margins, and cellular atypia. About 25% of cystosarcoma phyllodes are malignant by these criteria but only 25% of these metastasize. Metastases are usually to lung and bone but have been reported in every organ system. The metastases are always stromal and never epithelial.

The mortality rate is about 10% of all cases and is from metastatic disease. The tumor metastasizes hematogenously and not via lymphatics. Wide local excision should be adequate treatment for primary tumors and local recurrences. Simple mastectomy is suggested for large tumors or those with malignant characteristics. There is no rational behind axillary node dissection or pectoralis muscle resection unless this is required for adequate margins. Chemotherapy, hormonal therapy and radiation therapy have not been shown to have any affect on primary, recurrent, or metastatic disease.

SUMMARY

Cystosarcoma phyllodes is an uncommon tumor of the breast that demands wide local excision.

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Primary Carcinoma of the Gallbladder

A Retrospective Analysis

MMC and Mercy Hospitals 1957-1977

WILLIAM E. HERBERT, M.D.*

Primary carcinoma of the gallbladder is a recognized clinical entity usually discovered by surprise in one of two radically different settings. One is the so-called "incidental finding" which is found by the pathologist on routine sectioning of a cholecystectomy specimen. The other and unfortunately more common variety is the grossly obvious, advanced, inoperable lesion discovered by the surgeon at the time of laparotomy. This clinical dichotomy is probably more apparent than real, however, since, an intermediate form exists and is the basis for the surprisingly high cancer mortality rate in patients with so-called "incidental lesions" who were assumed to be cured by their cholecystectomy.^{1,2,4,6,7,8,9,11}

CLINICAL MATERIAL

Seventy patients with the diagnosis of primary carcinoma of the gallbladder treated at Maine Medical Center and Mercy Hospital during the twenty-year period 1957-1977 were included in the retrospective analysis. Ages ranged from 45 to 90, with an average age of 72 years. There were 52 females and 18 males. Sixty-six patients had surgery in one form or another and four patients had the diagnosis made at post mortem. The operations performed are listed on Table 1, the most common being laparotomy and biopsy. Fourteen patients had cholecystectomy only.

RESULTS

Fifty-seven patients (80%) had advanced disease at the time of diagnosis and all died within one year; the average length of survival was 3.8 months following diagnosis. Thirteen patients (20%) lived in excess of one year; four were diagnosed in the final year of this study and have no late follow-up. The remaining nine patients have survived two or more years since the time of diagnosis and are listed on Table 2. All of these patients had "incidental findings" of gallbladder cancer except patient #1 who had exophytic but not invasive tumor within the gallbladder and patient #9 who had the diagnosis made on biopsy of a distant site. Patients #1 through #6 have either died from other causes clinically free of disease or were alive without evidence of disease at the time of the study. Of particular interest are patients #7 and #8 who had "incidental lesions" having undergone routine cholecystectomy for cholelithiasis and were assumed to be cured of both ailments yet died two years later with liver metastases. In both of these patients, the

Table 1

Primary Gallbladder CA MMC & Mercy 1957 - 1977

Operations Performed		
GB-X	only	14
	& CDE	8
	& CDD	2
	& Gastroenterostomy	4
	& Hepatic a. 5-FU	2
	& CDD, hepatic res.	1
Cholecystostomy & bx.		6
Laporotomy & bx.		24
Misc:	Gastroenterostomy	3
	CDE & bx.	1
	CDD & gastroenterostomy	1
No operation (post only)		4
		<hr/> 70

Table 2

Primary Gallbladder CA MMC & Mercy 1957 - 1977

9 'survivors' > 2 years

*1) Alive	6 yrs.	F.O.D.	Hep. res., CDD
*2) Alive	4.5 yrs.	F.O.D.	GB-X
*3) L.T.F.	at 3 yrs.	F.O.D.	GB-X
*4) Dead	7 yrs.	F.O.D.	GB-X
*5) Dead	4 yrs.	F.O.D.	GB-X
*6) Dead	2 yrs.	F.O.D.	GB-ostomy
7) Dead	2 yrs.	Liver mets	GB-X
8) Dead	2 yrs.	Liver mets	GB-X
9) Dead	4 yrs.	Mediast. mets	Bx.

*Thus: 6/66 cured = 9%

early lesions were noted to be invading the muscularis layer of the gallbladder pathologically.

DISCUSSION

Primary carcinoma of the gallbladder is the most common biliary tract cancer, comprises 4% of all

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cancers, has a 3:1 female to male predominance and is encountered in approximately 1% of 'routine' cholecystectomies. It is a rapidly progressive disease, is rarely diagnosed preoperatively and carries a dismal survival rate. The etiology is not precisely known but there is a definite relationship to gallstones. Seventy-five percent of patients with carcinoma of the gallbladder have stones as well. Hamster experiments demonstrate a definite permissive role of gallstones in the development of gallbladder cancer. Polyps of the gallbladder are not etiologic.

Preoperative diagnosis is rare because the very early lesions produce signs and symptoms indistinguishable from those of cholelithiasis which is often co-existent. The very advanced lesion may present with mass, pain, jaundice, anorexia, and weight loss and mimics many other intra-abdominal malignancies. Radiological means including sonography, CT scanning, PTC and even angiography have not been helpful diagnostically due to lack of specificity. An exception to this is the finding of a "porcelain gallbladder" on x-ray, which is associated with a 25% incidence of gallbladder cancer.¹⁰

Pathologically, these lesions are mostly adenocarcinomas. The critical prognostic feature seems to be the microscopic level of invasion more than histologic grade of the tumor. The more undifferentiated lesions, however, seem to be the most invasive. Lesions confined to the mucosa should be cured by cholecystectomy alone but transmural lesions are virtually all fatal. Lesions invading the muscularis and no deeper are true intermediate lesions, not commonly encountered, but probably represent cases where radical surgery is indicated, i.e., cholecystectomy, wedge resection of the liver and regional lymphadenectomy. The anatomical basis for this radical surgery rests upon the unique and predictable mode of spread of this lesion. The most frequent spread is direct extension of the tumor into the liver via venous channels; widespread liver metastases are not seen because the venous drainage of the gallbladder only rarely has a direct connection with the portal system. Lymphatic spread is via the cystic duct node, porta hepatis nodes, superior pancreaticoduodenal nodes and ultimately the celiac nodes.^{1,3}

The experience in the literature has yielded consistently dismal results with this disease.^{1,2,4,7,8,9,11}

Specifically, the survival rate for patients with "incidental" lesions has been surprisingly low. In 166 patients with "localized" disease treated by cholecystectomy alone, there were only 30 five-year survivors (20%).¹² A 1970 review of the world literature, reviewing over 4,000 cases, showed that 27% of patients had what was thought to be a curable cholecystectomy but that only 10% of these patients lived 5 years.¹

As expected, the overall experience with radical surgery for gallbladder cancer is limited, reports of cures are sporadic, details of patient selections are not well outlined, and so it is not possible to draw any conclusions regarding its efficacy. It seems reasonable to speculate that patients with intermediately staged lesions would benefit from such surgery.

SUMMARY

Primary carcinoma of the gallbladder was diagnosed in seventy patients at Maine Medical Center and Mercy Hospitals in Portland, Maine from 1957 to 1977. Modes of treatment and survival data were retrospectively examined and found to be similar to other reported series. Our series confirms the unexpectedly high mortality rate in patients with "incidental" lesions and illustrates two cases of possibly overlooked intermediate lesions where radical surgery might have proven beneficial.

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Renal Artery Reconstruction

FERRIS S. ¹₁ I.D.*, RICHARD C. DILLIHUNT, M.D., ROBERT E. MCAFEE, M.D. AND
FREDERICK RADKE, M.D.

Continued refinements in surgical and angiographic techniques, better understanding of reno-vascular physiology and improved selection of patients allow surgeons to correct renal artery pathology that previously would have required nephrectomy. During the past 12 years, we have operated upon 38 patients with renal artery disease and our experience with this group is presented. Table 1 lists the five conditions for which surgery was performed.

RENO-VASCULAR HYPERTENSION (RVH)

Table 2 lists the clinical characteristics of patients with RVH. There was not a typical pattern of clinical presentation although headache was the most common symptom observed. All patients had been treated medically for various lengths of time with over two-thirds taking two or more drugs. Blood pressures ranged from 170/90 to 240/120 mm Hg., higher pressures being noted in patients with arteriosclerotic stenoses. Intravenous pyelograms were positive in only 40% of cases. Split renal function tests were not employed in the work-up of these patients and the final clinical selection for surgery was based on the results of renal arteriography and renal venous renin assay. Eight of 17 patients with arteriosclerotic lesions had positive renal vein renin assays, five of the eight patients with fibromuscular dysplasia had positive renal vein renin assays. Three patients had elevated peripheral renin determinations while nine patients did not have this hormone assay.

OPERATIONS

The various operations performed are shown in Table 3. Aorto-renal by-pass grafts utilizing autogenous saphenous vein was the most common operation. The durability of this graft has been proven by long-term angiographic studies in large series.^{1,2,3} When the renal artery lesion was on the left side, the splenic artery was utilized as a direct turnaround graft in four patients. In one case involving an obese male in whom a previous aorto-renal graft had been performed on the right side, a spleno-renal saphenous vein graft on the left was successful and avoided a difficult secondary exposure of the aorta.

RESULTS

In Table 4 the results during follow-up from 6 months to 12 years (average-33 months) are summarized. Two indices were used in evaluation: arm

TABLE 1

INDICATIONS FOR RENO-VASCULAR SURGERY	
Reno-vascular hypertension (RVH)	25
Renal salvage	5
Renal transplant stenosis	3
Renal artery trauma	3
Renal artery aneurysm	2
	38

TABLE 2

CLINICAL DATA OF PATIENTS WITH RVH			
Sex	Pathology		Avg Age
Female-13	Arteriosclerotic (AS)	17 (68%)	50
Male - 12	Fibromuscular hyperplasia (FMH)	8 (32%)	31
	Abdominal bruit	5 (20%)	
	AS	1	
	FMH	4	

TABLE 3

OPERATIONS PERFORMED FOR RVH			
AS (17)		FMH (8)	
Aortorenal SVG	12	Saphenous patch angioplasty	4
Spleno-renal arterial graft	4	Aortorenal SVG	3
Spleno-renal SVG	1	Aortorenal dacron graft	1
(SVG - saphenous vein graft)			

blood pressure values and the number of anti-hypertensive drugs required to maintain pressures in the range of normal. The best results were seen in the small group of patients with fibromuscular hyperplasia with seven of the eight patients (87%) felt to be cured or improved. Five patients have remained normotensive without medication and two patients require only one anti-hypertensive drug. The eighth patient has required two anti-hypertensive drugs for adequate control of blood pressure. The exact explanation for this failure is not clear. Of the 17 patients with arteriosclerotic stenoses, only nine (53%) were felt to be cured or improved. Although clinically better, five patients required more than one drug for adequate control of significant persistent hypertension. The most likely explanation for failure in this group is the probability of bilateral renal artery disease although only a few patients have been studied with follow-up angiography.

RENO-VASCULAR SURGERY FOR RENAL SALVAGE

Table 5 lists the clinical data of five patients who

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TABLE 4

RESULTS OF REVASCULARIZATION IN PATIENTS WITH RENO-VASCULAR HYPERTENSION (Follow-up avg—33 months)							
Preoperative				Postoperative			
AS (17)		FMH (8)		AS (14)		FMH (8)	
#Pt	#Drugs	#Pt	#Drugs	#Pt	#Drugs	#Pt	#Drugs
2	1	6	2	3	0	5	0
6	2	2	3	6	1	2	1
5	3			3	2	1	2
4	4			2	3		

(*cured or improved)

TABLE 5

SURGERY FOR RENAL SALVAGE—CLINICAL DATA					
Date	Pre-op Creatinine	B/P	Operation	Post-op Creatinine	B/P
1972 ♀ 58*	6.5	240/140	Lt renal end. Rt carotid end. ('77)	3.7	170/100
1973 ♂ 58*	2.8	220/110	Rt A-R SVG-Ilt nephrr. Lt carotid end. ('76)	1.7	150/80
1976 ♀ 59*	3.0	220/120	Rt A-R SVG-17 nephrr.	1.8	160/90
1978 ♀ 47	2.5	240/120	Lt spleno-renal	1.3	170/90
1978 ♀ 68	3.5	220/120	Rt carotid end. Rt ilio-renal SVG	1.2	150/80

(*Solitary Kidney)

had renal artery surgery for the primary purpose of renal salvage. In all patients, rapidly progressive renal insufficiency was noted with an elevated serum creatinine, severe diastolic hypertension and cardiac decompensation. One patient presented with a cerebral transient ischemic attack and required carotid endarterectomy prior to renal artery reconstruction. All patients had early angiography which revealed severe arteriosclerotic stenosis of the renal artery in four patients and complete thrombosis in one. Three patients had a solitary kidney and all patients were felt to be candidates for early dialysis if renal function could not be improved. Following reconstruction, steady improvement in serum creatinine levels and blood pressure was noted although all patients remained mildly hypertensive and required continued medical treatment. The longest follow-up has been over six years and all patients are still living with adequate renal function.

RENAL ARTERY TRAUMA

Three patients with renal artery trauma were explored. Two patients (ages 15 and 18) had unilateral artery trauma consisting of intimal laceration and one case (age 30) had bilateral traumatic renal artery thrombosis. The injury was identified in all cases by nonfunction with intravenous pyelography and confirmed by angiography. The two cases with unilateral trauma had associated splenic lacerations and were explored early (4 and 6 hours post injury). Both pa-

tients had splenectomy and vein patch graft angioplasty of the renal artery injury. Follow-up at 4 and 36 months reveals normal renal function in one patient and partial return of renal function in the other patient who remains normotensive. The diagnosis of bilateral renal artery thrombosis in a 30-year-old female was delayed (48 hours) and because of her general poor condition (chest injury, etc.) repair of only one renal artery was attempted. This was initially unsuccessful and the patient required renal dialysis for approximately three months at which time renal function returned and dialysis was discontinued. Recent renal scan and angiography reveals fair arterial flow through the repaired renal artery with evidence of moderate collateral circulation. In a review of the literature, Maggio and Brosman⁴ have correlated the success of surgery for renal artery trauma with the time between injury and operation. They noted success following repair done between 1.5 and 19 hours after injury while failure occurred following repairs from 16 to 84 hours after injury. From this data it would seem unwise to attempt renal artery repair in cases of *unilateral* injury later than 19 hours after injury. A small number of patients may develop delayed hypertension from intimal injury and subsequent renal artery stenosis. If properly identified, this group of patients could benefit from elective renal artery reconstruction. In patients with *bilateral* renal artery injuries, who otherwise do not represent prohibitive surgical risks, it would seem worthwhile

TABLE 6

RENAL ARTERY ANEURYSMS—SURGICAL INDICATIONS

- renal artery aneurysms > 1.5 cm.
- associated hypertension, fibromuscular hyperplasia, stenosis
- pregnancy
- ↑ size by serial angiograms

to attempt renal artery repair regardless of the time between injury and surgery.

RENAL ARTERY ANEURYSM

Although not common, renal artery aneurysms are being discovered more frequently with increased utilization of angiography for diagnostic purposes. We have operated on two renal artery aneurysms in female patients. One patient, age 39, was being evaluated for reno-vascular hypertension and was found to have a 2 cm. left renal artery aneurysm without associated pathology. This was treated by excision and primary anastomosis. The second patient, age 47, was being evaluated for gallbladder disease and a ring-like calcification was noted in the right upper quadrant separate from the gallbladder. Angiography revealed bilateral renal artery aneurysms associated with fibromuscular dysplasia of the proximal right renal artery. The larger aneurysm on the right measured 2.5 cm. This was treated by excision and vein patch angioplasty to correct the fibromuscular dysplasia. Both patients have continued to do well for two and nine years respectively.

Indications for surgery of renal artery aneurysms are listed in Table 6. These are not clearly defined and careful thought and individualization is necessary before recommending operative intervention. The treatment of asymptomatic renal artery aneurysms remains controversial but there is some evidence that aneurysms over 1.5 cm. and those associated with hypertension should be repaired.⁵ Renal artery aneurysms in females who may become pregnant are felt to be at higher risk for rupture and should be excised. Sensenig⁸ reported the results of treatment of two renal artery aneurysms he encountered within a two-year period at the Eastern Maine Medical Center. One patient underwent successful elective resection of a 2.8 cm. aneurysm while the second patient presented in shock and required a nephrectomy for a ruptured 6 cm. renal artery aneurysm.

POST-TRANSPLANT RENAL ARTERY STENOSIS

Following renal transplantation, three male patients developed poorly controlled hypertension followed by progressive renal insufficiency. Two patients had received cadaver kidneys and one patient a living donor kidney. Angiography revealed severe renal artery stenosis without signs of rejection. Surgical treatment consisted of renal artery angioplasty utilizing an onlay saphenous vein patch

graft. One patient has remained cured, one patient continues to be moderately hypertensive but with improved renal function and one patient has died of causes unrelated to surgery.

Post-transplant renal artery stenosis reportedly occurs in 1-10% of patients undergoing renal transplantation.^{6,7} Our known incidence at the Maine Medical Center has been three out of 90 transplants. Controversy concerning the etiology of stenosis in these cases continues with some authors feeling it is due to local trauma to the renal artery during perfusion or at the time of implantation and others feeling it is part of the rejection phenomenon. It is interesting that the stenosis does not occur at the arterial anastomosis but distal to this site. Treatment hinges on early diagnosis before renal function becomes impaired and prompt surgical correction.

SUMMARY

Experience with 38 cases having renal artery reconstruction has been presented.

The result of renal artery reconstruction in reno-vascular hypertension are best in patients with fibromuscular dysplasia although patients with arteriosclerotic lesions, if very carefully selected, should also benefit. A positive renal vein renin assay (ratio of 1.5 or greater) appears helpful in predicting a good result.

Although severe azotemia is unlikely to be the result of renal artery stenosis alone, there appears to be a small group of patients with rapidly progressive renal artery insufficiency and severe hypertension that may benefit greatly from renal artery repair when a correctable lesion is demonstrated by angiography.

Renal artery injuries secondary to trauma require prompt diagnosis and treatment for optimal results. Preservation of renal function is a universal goal but consideration of associated injuries and the general condition of the patient must temper aggressiveness toward renal artery exploration.

The recognition and surgical treatment of renal artery aneurysms and post-transplant renal artery stenosis have been discussed.

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Experience With Peritoneo-Venous Shunt

(LeVeen Shunt)

JAMES W. GEORGITIS, M.D. AND WALTER B. GOLDFARB, M.D.

INTRODUCTION

The word ascites is derived from Greek "Askos" or "bag." Ascites is a serious complication of cirrhosis, heralding the onset of extensive hepatocellular damage. Once uncontrolled ascites becomes manifest, death will occur in half of the patients in six months and within one year in two-thirds. When ascites persists, nutritional depletion, debility, and patient discomfort occurs. Associated problems occur because the ascitic patient has increased portal pressure and risks esophageal bleed, decreased lower esophageal sphincter pressure which predisposes aspiration, and gastric reflux which induces erosive esophagitis. Increased intra-abdominal pressure assists the development of hiatal, umbilical and inguinal hernia.

When medical therapy with diuretics fails, repetitive paracentesis depletes body protein, creates massive fluid and electrolyte shifts and risks the introduction of sepsis in a compromised host. Surgical therapy has been aimed at (1) increasing absorption of ascitic fluid (omentopexy, ileoentectomy), (2) reducing portal pressure (porto-caval shunts), and (3) diverting ascitic fluid into the venous system. Absorptive procedures were abandoned because of high mortality. Surgical therapy other than "bailing" by repetitive paracentesis has been in the form of porto-caval shunts. Given the often stormy postoperative course, financial burden of intensive care, drain upon blood reserves, and dismal outcome, it is no wonder that the internist is reluctant to submit his patients to surgical therapy even when medical therapy is inadequate. We initiated the use of the peritoneo-venous shunt as devised by LeVeen for the treatment of ascites to evaluate this mode of therapy hoping to avoid the surgical complications of more difficult procedures and provide some control for intractable ascites.

PHYSIOLOGY

An understanding of the pathogenesis of ascites is based upon Starling's hypothesis; the exchange of fluid across a capillary membrane is the result of hydrostatic pressure and osmotic gradients. Cirrhosis creates a venous outflow block which increases filtration of plasma from hepatic and visceral capillaries by raising hydrostatic pressure. Increased capillary permeability to protein creates a reservoir of albumin in a sequestered abdominal ultrafiltrate thus lowering the oncotic pressure differential. Intravascular

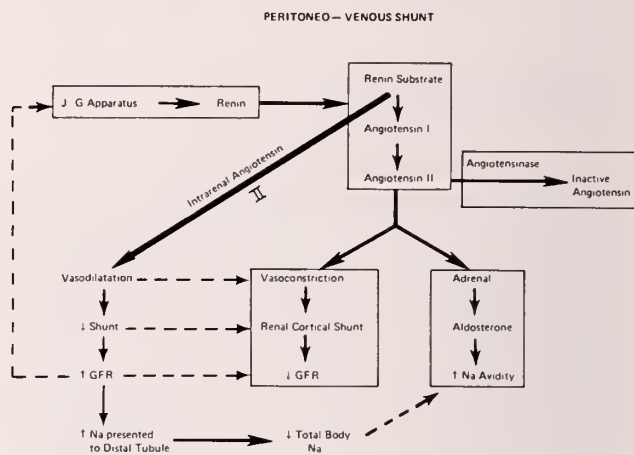


Fig. 1

hypoalbuminemia occurs further decreasing the transmural oncotic gradient. Hyponatremia ensues and further lessens the oncotic gradient. As ascites increases, the hepatorenal syndrome may develop with renal failure further augmenting ascities by decreasing urine output.³

The effect of a peritoneo-venous shunt is more complex than the simple shunting of this protein rich, high sodium content fluid from an intra-abdominal compartment to the intra-vascular compartment. The placement of a 3-5 cm pressure sensitive valve in a conduit between these two body compartments produces a diuresis and naturesis by a complex interaction with the kidney (Fig. 1).

Despite total body increase in sodium and excessive body water in the cirrhotic, renin and aldosterone levels are greatly elevated and marked sodium avidity present. It has been hypothesized that hyperaldosteronism and hyperreninemia develops from an imbalance of lymph formation and lymph absorption. Increased venous pressure behind the outflow block of nodular cirrhosis increases fluid filtration by hepatic and splanchnic capillaries. Despite high flow through the thoracic duct, lymph return is insufficient and ascites results. Decrease lymph return may stimulate increased renin levels through volume or oncotic effect. Renin released from the juxtaglomerular apparatus in turn activates a vasoactive peptide angiotensin. Angiotensin is converted to angiotensin II. Angiotensin II effects renal cortical blood flow and causes a diminution of GFR. It also stimulates adrenal production of aldosterone which increases absorption of the sodium from the distal tubule.

Decreased renal cortical perfusion occurs when

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one component of the renin-angiotension system is altered. Low plasma renin substrate which is the precursor to angiotensin has been shown in isolated kidney perfusate to redistribute renal blood flow. Instead of renal cortical shunting of blood, parenchymal perfusion is increased. It is felt that the substrate is converted to intrarenal angiotension II. In turn, this redistributes blood flow establishing parenchymal perfusion and increasing GFR. Isolated perfusion of the kidney with angiotensin II caused renal artery vaso-constriction. Experimental similarities of this effect and the effect of Aramine, a vasoconstrictor which improves renal perfusion has been noted.^{1,2}

Following insertion of the P-V shunt, creatinine clearance increases in 50% of patients. However, these same patients may fail to respond with diuresis when given volume expansion with electrolyte solution or colloid solution. This puzzling physiological response has been partially elucidated by the preceding clinical and experimental investigations.

In hepatorenal syndrome, it is not the kidney which is at fault. It is well known that these kidneys can be transplanted and function well. With the introduction of the P-V shunt, they also have return of function. This apparent paradoxes can be explained by two factors. One is the return of "spilled lymph" from the sequestered intra-abdominal compartment to the intravascular compartment which increase colloid volume and restores lymphatic dynamics.

The second factor is change of the renal-endocrine dynamics. Ascitic fluid contains a renin substrate in concentrations 25-50% of plasma levels. Given the large volume of ascites an absolute large amount of substrate can be presented to the kidney for generation of intrarenal angiotensin II for re-establishment of parenchymal blood flow and improvement in GFR. Increase in GFR would in turn inhibit renin and aldosterone secretion.

Other mechanical factors may assist the increased production of urine. The alleviation of compression on the intra-abdominal vena cava by decreased ascites may decrease renal vein back pressures and improve renal function.

Less well studied components of this problem may be the hyper-dynamic cardiac state that occurs due to the enlarged vascular space and numerous arterio-venous fistulas (intrahepatic, spider angiomas, etc.) This creates an increase in capacitance and decrease in resistance resulting in decreased blood pressure and decreased renal blood flow.^{4,5,6,7,8,9,10,11}

INDICATIONS

Criteria for selection of patients, to undergo this procedure are still debatable. In general, we have selected patients who have massive, disabling ascites with stable liver disease. They must have failed to improve their ascites on medical management. Specifically, an abstention from hepatotoxic agents (ETOH), sodium restriction (500-1, 500 mg Na diet), diuretic therapy (Aldactone® 25 mg Q.I.D., and

either ethacrinic acid or furosemide), and fluid restriction (a liter a day) over a two to six-week period. Ascitic fluid should be free of infection (afebrile patient, ascitic fluid with WBC of less than 400 cells/mm).³ Most of the patients in this series were also previously evaluated by a gastroenterologist.

CONTRAINDICATIONS

The peritoneo-venous shunt is not recommended in patients with severe alcoholic hepatitis with bilirubins greater than 8-10 mg/dl. Encephalopathy, acute tubular necrosis and peritoneal sepsis are contraindications to shunt placement. Cardiac disease is a constraint and requires digitalization and initiation or continuation of diuretic prior to P-V shunt placement. Severe bleeding diathesis and previous esophageal varices which have bled are contraindications to P-V placement.

PATIENT PREPARATION

Aside from a basic physical exam, cardiac, pulmonary, renal function evaluation, special attention is placed on inspecting the route of the catheter from the abdomen to neck to ensure that no localized skin infections or previous surgical incisions would preclude safe passage of the catheter. Preoperative assessment of patency of the external jugular vein is evaluated by inspection.

Preoperative digitalization and on call three dose schedule antibiotics (Cefazolin 1 Gm) is given. Base line arterial blood gas and preoperative incentive spirometer training is provided by the respiratory department to assist in the development of a thoraco-abdominal pressure gradient to increase shunt flow. Preoperative weight and girth are recorded. Electrolyte status, liver profile and coagulation parameters are measured. Ascitic fluid is removed for protein, specific gravity, LDH, amylase, cell count, and culture. EKG and preoperative chest film are obtained. The patient is typed and crossmatched for two units of packed cells. A pHisoHex® bath is ordered and an indwelling Foley catheter is placed with an attached hourly urometer prior to the operation.

POSTOPERATIVE CARE

Postoperatively, a chest film is taken in the recovery room to establish a base for diuretic management if pulmonary edema should occur and to check catheter placement. The patient has a 6-hour postoperative serum K⁺ and Na⁺, hematocrit and hemoglobin measured as well as hourly I & O recordings. Further electrolyte and blood values are ordered as required.

Diuretics may be given as intermittent bolus via soluset to initiate diuresis if required. An abdominal binder is applied on the second postoperative day and incentive spirometer therapy started to encourage a thorax-peritoneal pressure differential. Daily weights and abdominal girth are measured until discharge.

Wound healing in these protein depleted patients is slow and sutures are left for at least two weeks unless inflammatory reaction is present. Discharge from the hospital is usually in two weeks and the patient is instructed to continue use of the abdominal binder; diuretics may or may not be necessary. Sodium and fluid restriction is not usually required. Digitalis is continued for six weeks and follow-up appointment at monthly intervals arranged.

OPERATIVE PROCEDURE

Anesthesia is either general or 1% Xylocaine® with intravenous Oxazepam (Serax®) which is better handled by the injured liver than Diazepam (Valium®). The patient is supine, prepped with Betadine® from ear lobe to lower abdomen and draped. A 10 cm transverse incision is made in the right upper quadrant below the liver edge if it is palpable. The incision is carried through the anterior rectus sheath; rectus muscle is split to expose the posterior rectus fascia. Cautery is used for hemostasis. A counter wound is made in the anterior rectus sheath for the conduit tubing. Two silk-00 sutures are placed circumferentially in the posterior rectus sheath. A stab wound is made and the peritoneal component (.32" silastic tube with 16 staggered holes) of the shunt is rapidly introduced into the abdomen and sutures secured rapidly to minimize ascitic loss. The conduit tubing is clamped and brought through the counter wound of the anterior rectus fascia. The anterior rectus fascia is then approximated with 000 interrupted silk.

A longitudinal incision parallel to the anterior border of the sternocleidomastoid is made, carried through subcutaneous tissue and platysma to expose the sternocleidomastoid. Sharp dissection and reflection of the muscle laterally exposes the internal jugular vein. A facial branch may be sacrificed to gain further exposure. Careful dissection around the vein and passage of two 0-silk ties with care taken not to entrap the vagus nerve or recurrent laryngeal is completed. This allows traction for the placement of the venous end of the shunt.

A tunnel is then bluntly dissected from the abdominal wound to the rib margin, brought to the right of the nipple into the neck wound. Bronchoscopy biopsy forceps may assist in passage of the umbilical tape to which the distal end of the conduit tubing has been sutured. The tube is clamped adjacent to the valve and drawn through the tunnel. Counter wounds to assist the passage of the umbilical tape may be made. The conduit is trimmed so that approximately 3 cm will be intravenous below the angle of the sternum. A venotomy is made, tubing inserted, and ligatures secured.

The cervical wound is closed with interrupted 0000-dexon and a running subcuticular suture. The abdominal wound is closed with 0000-dexon subcuticular and 0000-nylon. Dry dressings are applied with hypoallergenic paper tape to prevent damage to the fragile skin.

RESULTS

In our series of nine patients, a total of ten peritoneo-venous shunts were placed. Three were males, and six were females with an average age of 59 years. Five had intractable ascites from Laennec's cirrhosis, one from non-alcoholic post-necrotic cirrhosis, one from biliary cirrhosis resulting from common duct stricture and two from malignant ascites.

These patients were symptomatic with dyspnea, immobile from the sheer mass of ascites and malnourished. One patient experienced dramatic relief of miralgia paraesthetica from impingement of the femoral cutaneous nerve between the ascitic abdomen and the inguinal ligament when her ascitic was resolved.

The average postoperative weight loss was 14.3 kg by the 10th postoperative day. Abdominal girth decreased an average of 22 cm.

We sensed a general improvement in CNS status but were unable to quantify this impression. An explanation for this has recently been suggested. Production of antibodies against endotoxins is markedly elevated in post P-V shunt patients. These antibodies may be protective against the toxic effects of increased endotoxemia seen in cirrhotic patients.

COMPLICATIONS

The most common complication encountered in our series was failure to maintain shunt patency. Approximately 10-20% of shunts have occlusion occur from fibrin deposits. Usually this becomes apparent by reaccumulation of ascites, rapid weight gain, and increasing abdominal girth. Decreased urine output, increasing respiratory difficulty and hyponatremia suggest shunt failure. Rarely does the valve fail, but more often fibrin deposit occlude either the peritoneal or venous ends.

Occlusion can be assessed by intraperitoneal instillation of 5 millicuries of 99m Tc-sulfur colloid. Scintillation camera scans at 30 minutes and one

TABLE 1

PERITONEO-VEIN SHUNT		
No. Pt.		9
No. Shunts		10
Sex	3 —	6 —
Average Age		59 years

TABLE 2

PERITONEO-VEIN SHUNT	
Complications	
Occlusion	3
Erosion	2
GI Bleed	3
Pulm. Edema	1
U.T.I.	1
Death	1

TABLE 3

PERITONEO-VEINUS SHUNT

Etiology of Ascites

Diagnosis	
Biliary cirrhosis	1
Post necrotic cirrhosis	1
Carcinomatosis	2
Laennec cirrhosis	5

TABLE 4

PERITONEO-VEINUS SHUNT

Symptoms

Bedridden	8
Dyspnea	3
Miralgia Paresthetica	1
Prolapsed umbilicus	1
Failed medical therapy	9
Decubitus	2

hour may show progression of the nucleotide through the shunt. If the nucleotide fails to reach the superior vena cava, renographin may be injected with a 23 gauge needle into the tubing to document venous and patency.¹² Intra-operatively, Methylene Blue may be injected and observed to progress up the shunt conduit assuring patency. In large series, it has been noted that patients with fibrin split products greater than 1:512 will have a higher incidence of shunt occlusion.

Other major complications are electrolyte disturbance, pulmonary edema, bleeding diathesis and hepatic coma. Pulmonary edema and congestive heart failure can be avoided by preoperative digitalization and immediate postoperative fluid restriction during this massive diuresis phase of recovery. Some patients have persistently hour urines of greater than 300 ml. Hypokalemia may be a consequence of this massive diuresis. Leakage of ascites through the abdominal wound often encountered can be controlled by meticulous attention to wound closure.

We have encountered more complex postoperative problems. Gastrointestinal hemorrhage occurred in

three patients but none were associated with a DIC coagulopathy as has been reported in the literature. One patient had significant pulmonary edema requiring intensive care management for 24 hours. Two patients eroded components of the shunt through the skin over a six-month period. One patient died from sepsis (staph pneumonia) and gastrointestinal hemorrhage with a patent shunt.

SUMMARY

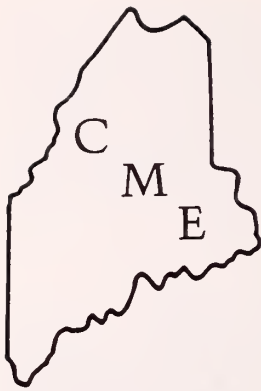
The exact physiologic effect of the P-V shunt remains to be clearly elucidated. Candidates for this procedure are not clearly defined, but diuretic-resistant cirrhotics have had excellent results. We have had good success with malignant ascites. Careful selection, close adherence to pre and postoperative care is required for successful outcome. Complications are more frequent than noted in the literature and long-term benefits are yet to be determined.

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CONTINUING MEDICAL EDUCATION IN MAINE

Conferences and Workshops

Title: Rectal Colon Cancer and Cancer of the Lung
Date: November 12, 1980, 8:30 a.m.-5:00 p.m.
Location: Nasson College, Springvale, Maine
Sponsors: American Cancer Society, Maine Affiliate, H.D. Goodall Hospital, and York County Medical Society
Credit: AMA and LCCME Category I—8 hours and AAFP (applied for)
Reg. Fee: To be determined

Title: Teaching and Instructional Skills Workshop for Physicians
Date: November 14-16, 1980
Location: Sheraton Inn, South Portland
Sponsor: Medical Care Development
Credit: AMA and LCCME Category I—14 hours and AAFP (Prescribed)—14 hours
Reg. Fee: \$95

2nd Tues.	Pulmonary Medicine Section Conf.	8-9 a.m.
3rd Tues.	Dermatology-Pathology Conference	5-6 p.m.
3rd Tues.		
1st Wed.	Ophthalmology Section Meeting	7:30-8:30 p.m.
1st Wed.	Tumor Clinic Conference	2-5 p.m.
1st Wed.	Radiology Conference	5-6 p.m.
2nd Wed.	Tumor Clinic Conference	2-5 p.m.
2nd Wed.	Radiology Conference	5-6 p.m.
3rd Wed.	Tumor Clinic Conference	2-5 p.m.
3rd Wed.	Radiology Conference	5-6 p.m.
4th Wed.	Tumor Clinic Conference	2-5 p.m.
4th Wed.	Radiology Conference	5-6 p.m.
1st Thurs.	Ophthalmology Section Meeting	7:30-8:30 a.m.
1st Thurs.	OB-GYN Conference	8-9 a.m.
1st Thurs.	Pediatric Grand Rounds	9-10 a.m.
1st Thurs.	Medical Service Meeting	10-11:15 a.m.
1st Thurs.	Cardiology Conference	11 a.m.-1 p.m.
2nd Thurs.	OB/GYN Conference	8-9 a.m.
2nd Thurs.	Pediatric Grand Rounds	9-10 a.m.
2nd Thurs.	Medical Service Meeting	10-11:15 a.m.
2nd Thurs.	Cardiology Conference	11 a.m.-1 p.m.
2nd Thurs.	Surgical Service Meeting	7:45-9 a.m.
3rd Thurs.	OB/GYN Conference	8-9 a.m.
3rd Thurs.	Pediatric Grand Rounds	9-10 a.m.
3rd Thurs.	Medical Service Meeting	10-11:15 a.m.
3rd Thurs.	Cardiology Conference	11 a.m.-1 p.m.
4th Thurs.	OB/GYN Conference	8-9 a.m.
4th Thurs.	Pediatric Grand Rounds	9-10 a.m.
4th Thurs.	Medical Service Meeting	10-11:15 a.m.
4th Thurs.	Orthopedic Service Meeting	7:30-9 a.m.
4th Thurs.	Urology Section Meeting	7:30-8:30 a.m.
4th Thurs.	Surgical Service Death Review	7:45-9 a.m.
1st-4th Fri.	Neurology Grand Rounds	8-9 a.m.

Hospital Activities

Augusta Mental Health Institute Augusta, Maine

Nov. 20, 1980
10-11:30 a.m. **Psychological Testing I**
Jane Thorbeck, Ed.D., Harvard Medical School; Massachusetts General Hospital

Dec. 4, 1980
10-11:30 a.m. **The Violent Patient**
Park Dietz, M.D., McLean Hospital; Harvard Medical School

Dec. 11, 1980
10-11:30 a.m. **Special Issues in Family Therapy Training**
Leonard Siegel, M.D., Augusta Mental Health Institute

Dec. 18, 1980
10-11:30 a.m. **Possible Genetic Sensitivity to Hallucinogens—Drugs**
Henry Abraham, M.D., Harvard Medical School; Massachusetts General Hospital

These sessions are Grand Rounds. All programs have been certified AMA and LCCME Category I. For further information contact Pauline Soper; 622-3751.

Eastern Maine Medical Center Bangor, Maine

1st Mon.	EEG Conference	12-1 p.m.
1st Mon.	Weekly Surgical Service Rounds	5-6 p.m.
2nd Mon.	EEG Conference	12-1 p.m.
2nd Mon.	Weekly Surgical Service Rounds	5-6 p.m.
3rd Mon.	EEG Conference	12-1 p.m.
3rd Mon.	Weekly Surgical Service Rounds	5-6 p.m.
4th Mon.	EEG Conference	12-1 p.m.
4th Mon.	Weekly Surgical Service Rounds	5-6 p.m.
4th Mon.	ENT Section Meeting	12-1 p.m.
1st Tues.	Surgical Service Review Meeting	12-1 p.m.
2nd Tues.	Family Practice Service Meeting	6:30-7:30 p.m.

Visiting Professor Program:

2nd Thurs.	Medical Service Visiting Professor	10 a.m.-5 p.m.
4th Thurs.	Pediatric Service Visiting Professor	10 a.m.-5 p.m.
as scheduled	Surgery Service Visiting Professor	
as scheduled	Orthopedic Service Visiting Professor	
as scheduled	Family Practice Visiting Professor	
as scheduled	Psychiatric Service Visiting Professor	
as scheduled	OB/GYN Service Visiting Professor	

Nov. 13, 1980
7-8 a.m. **Anesthesia Service Visiting Professor**

All activities have been certified AMA and LCCME Category I. For further information contact James F. Lawsing, III, M.D.; 947-3711 Ext. 2303.

Henrietta D. Goodall Hospital Sanford, Maine

Nov. 18, 1980 **The Management of Diabetic Complications**

Thomas Flood, M.D., Harvard Medical School, Boston, Massachusetts

Dec. 18, 1980

Office Dermatology

Douglas Wooldridge, M.D., Harvard Medical School, Boston, Massachusetts

These meetings will be held at the H.D. Goodall Hospital's Conference Room at 7 p.m. These programs have been certified AMA and LCCME Category I, AAFP (applied for) and Maine Pharmaceutical Association credit. For further information contact Melvin Bacon, M.D.; 324-3632.

A. R. Gould Memorial Hospital Presque Isle, Maine

Nov. 17, 1980

Hypnosis in Psychological Medicine

Robley Morrison, Ph.D., A.R. Gould Memorial Hospital

Nov. 24, 1980

Breast Cancer/Head Injuries

Jean Labelle, M.D., Maine Medical Center

Dec. 1, 1980

Differential Diagnosis and Treatment of Tremors

George Wright, III, M.D., Eastern Maine Medical Center

Dec. 8, 1980

Management of Congestive Heart Failure

Paul Minton, M.D., Maine Medical Center

Dec. 15, 1980

Sidney Farber Cancer Institute Speaker

These meetings are Grand Rounds and begin at 7:30 p.m. in the Rotary Regional Educational Center at A.R. Gould Memorial Hospital. These programs have been certified AMA and LCCME Category I. For further information contact Marilyn Dean; 769-2511.

Kennebec Valley Medical Center Augusta, Maine

Oct. 28, 1980

Pelvic Pain

7:30-8:30 a.m.

John Rampone, M.D., Bay State Medical Center, Springfield, Massachusetts
Grand Rounds

This program has been certified AMA and LCCME Category I and AAFP (Prescribed). For further information contact Nancy Favorite; 623-4711, Ext. 333.

Mid-Maine Medical Center Waterville, Maine

Nov. 13, 1980

Orthopedic Surgery

Stuart Belkin, M.D., Tufts University School of Medicine

Nov. 18, 1980

Multiple Gestation

John Makin, M.D., Rumford Community Hospital
ITS Presentation

Nov. 20, 1980

Renal Transplant

Donald Leeber, M.D., Maine Medical Center

Nov. 25, 1980

Toxemia—Pre-Eclampsia

Herbert Bartholomew, M.D., Kennebec Valley Medical Center—ITS Presentation

Dec. 4, 1980

Clinical Pathological Conference

(Medical Staff Only)

Dec. 11, 1980

Endocrinology

Hugh Johnston, M.D., Maine Medical Center

Dec. 16, 1980

Diabetes in Pregnancy

Paul Jones, M.D., Mid-Maine Medical Center—ITS Presentation

Dec. 18, 1980

Gynecologic Out-Patient Surgery

John Makin, M.D., Rumford Community Hospital

The above activities are from 12-1 p.m. and have been certified AMA and LCCME Category I. For further information contact David Ginder, M.D.; 873-0621.

LETTER TO THE EDITOR—Continued from Page 325

after treatment was started. In this series, the results were mixed. Although one patient's symptoms were relieved by cimetidine in the setting of refractoriness to another drug, a second patient responded to diphenylhydramine but not to cimetidine. In the third patient, the pruritus was not responsive to any of the drugs.

From the available studies, it appears that cimetidine may be of benefit for pruritus in some patients with polycythemia vera and Hodgkin's disease. Its further study in a controlled fashion may define its effectiveness and allow for the elucidation of the mechanism of pruritus in patients with the hematologic disorders. It is intriguing that both H_1 and H_2 histamine receptors are found on thrombocytes and are related to lymphocyte function.⁷ Cimetidine may be a reasonable alternative for short-term use in patients with pruritus. Its usefulness in patients refractory to other anti-pruritic agents has not been established.

REFERENCES

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DELYN C. CASE, JR., M.D., F.A.C.P.
Divisions of Hematology and Oncology
Maine Medical Center
Portland, ME 04102

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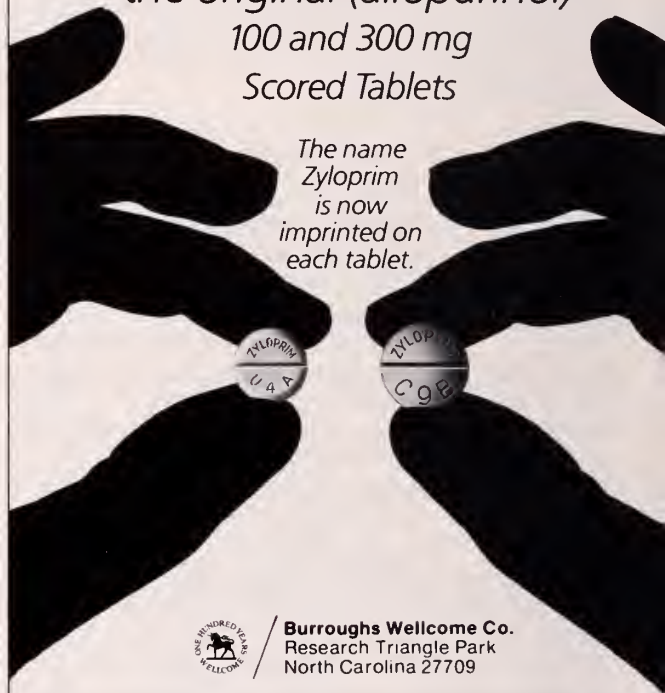
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The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma, may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication. Abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported, should these occur, discontinue drug. Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long-term therapy.

Dr. Richard C. Wadsworth, 74, of Bangor, Maine, died on September 8th at a Bangor hospital.

He was born on September 9, 1905 in Framingham, Massachusetts, the son of George A. and Flora B. Wadsworth.

Dr. Wadsworth was graduated from Cornell University and received his medical degree from the University of Rochester School of Medicine in 1931. He interned at the Strong Memorial Hospital in Rochester, New York and following a two-year residency in pathology at the Newark Beth Israel Hospital in New Jersey, he joined the faculty of pathology at Tufts University Medical School.

From 1938 to 1942, he was pathologist at the Metropolitan State Hospital in Waltham, Massachusetts. He served in the U.S. Army Medical Corps as the director of the laboratory of the Army's 148th General Hospital in the Pacific Theatre from 1942 to 1945 as a Lt. Colonel. In 1946, he located in Bangor where he was affiliated with the Eastern Maine Medical Center and was head of the Stoddard Laboratory at the hospital from 1947 through 1972 and had continued his work at the hospital's tumor clinic until recently.

Dr. Wadsworth was a senior member of the Penobscot County Medical Society, the Maine Medical Association and the American Medical Association. He was also a member of the College of American Pathologists and the American College of Physicians.

Surviving are his widow, Mabel A. Wadsworth; three daughters, Rachael W. Pooler, Janet W. Pease and Martha W. Leighton; two brothers, Robert K. of Framingham, Massachusetts and Philip P. of Winchester, Massachusetts; four granddaughters; one grandson; and several nieces and nephews.

County Society Notes

Androscoggin

The May meeting of the Androscoggin County Medical Association was held at Chase Hall, Bates College in Lewiston on May 15, 1980 with 40 members present.

The meeting was called to order at 7:15 p.m. by the President, Dr. Leo E. Cousineau.

Printed minutes of the meeting of April 17, 1980 were distributed and accepted.

A moment of silence was observed for deceased member Dr. Ralph Goodwin, Sr. A memorial resolution for Dr. Goodwin was then presented by Dr. Waldo Clapp. This resolution was accepted as a part of the permanent records of the ACMA and a copy will be sent to Dr. Goodwin's family.

Dr. Walworth reviewed the correspondence which included a letter from Governor Brennan.

Dr. Walworth then gave a brief report on the Executive Committee meeting of May 6, 1980.

Dr. Holler reported on the Health Care Finance Committee and reviewed the agenda for the M.M.A. annual meeting as well as reviewing the proposed Code of Ethics. The majority of the members present indicated their preference for the existing Code as opposed to the proposed revision.

Dr. Cousineau gave an update on the status of the Preliminary State Health Plan.

A report of the Advisory Committee was given by Dr. Michael Rynne.

The meeting was adjourned at 8:15 p.m.

A meeting of the Androscoggin County Medical Society was held on June 19, 1980 at Chase Hall, Bates College in Lewiston, Maine, with 41 members present.

Printed minutes of the meeting held May 15, 1980 were

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Number 12

High-Dose Methotrexate With Citrovorum Factor Rescue for Patients With Refractory Lymphoproliferative Disorders

DELVYN C. CASE, JR., M.D., F.A.C.P.*

ABSTRACT

Twelve consecutive patients (ages 20-67) with advanced refractory lymphoproliferative disorders were treated with high-dose methotrexate and citrovorum factor rescue to study the drug's effectiveness and dose response. Treatment was begun at 250mg./m² and escalated to 3gm./m². Therapy was given every two weeks. Six of the twelve patients responded. Five of the responses were partial with only brief durations; however, one patient has had a complete remission lasting for longer than one year. Responses were noted in nodes, liver, spleen, and bone marrow. Two of the three patients with CNS disease refractory to corticosteroids and radiotherapy responded to systemic methotrexate. Toxicity was minimal. Although the responses were brief in this refractory group of patients, methotrexate used in high doses may have promise in newly diagnosed patients with lymphomas to add to the armamentarium of effective drugs for systemic therapy and also as drug for CNS prophylaxis.

INTRODUCTION

Combination chemotherapy programs have significantly contributed to the remission rate and survival of patients with advanced non-Hodgkin's lymphoma.¹⁻³ The three drug regimen, cyclophosphamide, vincristine and prednisone produces complete remissions in 77% of patients with nodular histology.⁴ With the addition of bleomycin and doxorubicin (Adriamycin) both independently active in the non-Hodgkin's lymphomas,⁵⁻⁸ the complete response in the diffuse poorly differentiated lymphocytic, histiocytic and mixed groups, all un-

favorable histologies, has been improved to 50-90%.⁹⁻¹¹

Despite a high initial response rate, a significant number of patients sustain a recurrence of their disease. High-dose methotrexate followed by citrovorum factor rescue (HD-MTX/CF) was introduced by Djerassi, in 1967, in children with acute lymphocytic leukemia.¹² Others have confirmed the improved therapeutic index compared with prior experience with methotrexate at conventional doses in lymphomas¹³⁻¹⁴ and a variety of other malignancies.¹⁵⁻¹⁸ The toxic effects of the HD-MTX can be reversed by timely administration of citrovorum factor rescue; extremely high doses (3.0-7.5g/m²) of MTX can be administered safely and the myelotoxicity and mucous membrane lesions characteristic of MTX toxicity prevented.¹⁹⁻²⁰ Furthermore, pharmacologic investigations of cerebrospinal fluid (CSF) concentrations of MTX have demonstrated that the higher dose MTX regimens can result in cytotoxic concentrations in spinal fluid after systemic administration of the drug.²¹ For planning of newer chemotherapeutic programs for non-Hodgkin's lymphomas, HD-MTX/CF would be appealing to administer the agent with myelotoxicity and use as prophylactic treatment for the prevention of central nervous system (CNS) relapse.²²

The purpose of this report is to evaluate the results of HD-MTX/CF in patients with refractory lymphoproliferative disorders to explore the potential usefulness and toxicity of the drug program particularly for its CNS effect.

MATERIALS AND METHODS

The clinical and pathologic characteristics of the 12 patients with advanced disease are shown in Table 1. Histopathology was categorized according to the

*Divisions Hematology and Oncology, Department of Medicine, Maine Medical Center, Portland, Maine 04102.

TABLE 1

	Age	Sex	Histology	Stage	Extranodal Sites	Prior Therapy*	Doses of HD-MTX/CF (mg/m ²)	Response to HD-MTX/CF
1.	23	M	NPDL	IV	Marrow	COP, A, Bleo, BCOPM, XRT	250-3000	NR
2.	23	F	DPDL	IV	Marrow	CAOP-Bleo	250-3000	PR (2 mo)
3.	20	M	DPDL	IV	Marrow	CAOP-Bleo	250-3000	NR
4.	65	M	DHL	IV	CNS	CAOP-Bleo	250-3000	PR (2 mo)
5.	45	F	NPDL	IV	Marrow	COP, BCOPM	250	PR (3 mo)
6.	50	F	NPDL	IV	Marrow, CNS	COP, BCOPM	250	PR (3 mo)
7.	21	M	DPDL	IV	Bone, Liver, spleen	CAOP, asparaginase	250	NR
8.	63	F	DWDL	IV	Marrow	COP, BCOPM	250	CR (12 + mo)
9.	67	F	DWDL	IV	Marrow, Liver, CNS	COP, BCOPM	250	NR
10.	65	M	CLL	IV	Marrow, Liver, spleen	Chlorambucil, COP, BCOPM	250	PR (1 mo)
11.	30	M	Hodgkin's	III		MOPPro/ADV, Bleo	250	NR
12.	50	M	Hodgkin's	III		MOPPro/ADV, Bleo	250	NR

*C (cyclophosphamide), O (Oncovin®), P (prednisone), A (adriamycin), Bleo (bleomycin), M (melphalan), B (B.C.N.U.), M (mustard), P (procarbazine), D (decabazine), V (vinblastine), XRT (radiotherapy).

Rappaport classification.²³ Histologies included nodular poorly-differentiated lymphocytic lymphoma (NPDL) (3), diffuse poorly-differentiated lymphocytic lymphoma (DPDL) (3), diffuse histiocytic lymphoma (DHL) (1), chronic lymphocytic leukemia (CLL) (1), diffuse well-differentiated lymphocytic lymphoma (DWDL) (2), and Hodgkin's disease (2). The median age was 45 years (range 20-67). All patients were evaluable; no patient was excluded because of early death.

All patients were heavily pre-treated on initial treatment protocols (Table 1). None of the patients who relapsed in the CNS had prior prophylactic intrathecal methotrexate therapy or radiation. Informed consent was obtained.

Patients were required to have a creatinine clearance greater than 60ml/min. (except one case). Alkalinization of the urine was achieved by administration of sodium bicarbonate 3g. by mouth every three hours beginning 12 hours before HD-MTX and continuing for 48 hours thereafter.²² HD-MTX was administered intravenously at an initial dose of 250mgs./m² and escalated to 3gm./m² if toxicity did not develop at the lower previous dose. CF (10mg./m²) was administered intravenously 24 hours after HD-MTX and continued at 10mg./m² orally every 6 hours for 72 hours. Treatment was discontinued if subsequent pre-treatment BUN and creatinine were abnormal or if significant hematologic or mucosal complications occurred as a result of elevations of renal parameters during treatment. Therapy was planned for every two weeks until complete response occurred and then monthly for a total of 12 monthly treatments as long as complete remission continued.

Complete response (CR) was defined as the com-

plete regression of all measurable disease for at least one month. Partial response (PR) was defined as greater than 50% reduction in measurable lesions lasting at least one month. Non-responders (NR) included patients who progressed on treatment or those that had less than 50% regression. Response duration was measured from the time of achieving maximal response to the time of relapse. Responses were confirmed by physical examination, x-ray study, bone marrow aspiration/biopsy, and spinal fluid evaluations.

RESULTS

HD-MTX/CF was administered to 12 patients with refractory lymphoproliferative disorders. Of the 12 patients, 6 responded. Five of the responses were PR and one was CR. A median of 6 doses was administered. Doses of HD-MTX were escalated in the first 4 patients up to 3000mg./m² without additional benefit. Therefore, the dose of HD-MTX was not escalated in the remaining 8 patients.

Disease regression occurred rapidly with most responses evident with 1-3 doses. If a patient did not respond after 4 doses, subsequent doses did not produce a remission. Responses were noted in nodes, liver, spleen, bone marrow and CNS. All histologies responded except for 2 patients with Hodgkin's disease. The duration of remissions in the PR group was disappointingly short (1-3 months) and probably reflected the disseminated and refractory state of the underlying disease. The one patient with a CR has had a remission for 12+ months. This patient with DWDL and extensive bone marrow disease responded promptly and completely. Her case was complicated by unrelated, previously diagnosed proliferative glomerulonephritis with a creatinine

TABLE 2

HD-MTX/CF THERAPY OF CNS LYMPHOMA

<i>Histology</i>	<i>CSF Cytology</i>	<i>CNS Response to HD-MTX/CF</i>
NPDL	+	PR (2 mo)
DHL	+	PR (3 mo)
DWDL	+	NR

clearance pf 20cc./min. With CF given IV q. 6 hours for the full number of doses, renal function was preserved.

The response to systemic HD-MTX/CF in 3 patients with CNS disease refractory to steroids and radiotherapy was revealing (Table 2). Two of the three patients responded. One of the 2 patients who responded received HD-MTX up to 3gm./m²; however, the initial improvement was to the 250mg./m² dose. Escalation of the dose of HD-MTX did not improve the response. The second patient responded to the 250mg./m² dose which was continued until relapse. Both responses were only partial and temporary. The two patients had achieved only partial responses systemically and relapsed concurrently in nodes, CNS, and marrow. Treatment was given every two weeks as in the cases without CNS involvement.

Side effects were minimal and independent of the dose of HD-MTX. Significant myelosuppression did not occur; treatment was given in patients with compromised marrow and depressed counts prior to therapy. Three patients had nausea and vomiting and two had mucositis. None of the patients developed renal insufficiency or had treatment discontinued because of renal deterioration. One patient with DWDL was treated with abnormal creatinine clearance at onset, presenting with a prior history of proliferative glomerulonephritis. HD-MTX/CF therapy was offered because of the lack of other available effective treatment. Use of IV CF spared renal function. The serum level of HD-MTX was in this patient 1x10⁻⁶m at 24h and toxicity did not develop with CF therapy. Her CR has now been 12+ months; treatment is to be discontinued.

DISCUSSION

In the present study, HD-MTX/CF has been shown to produce responses in a group of heavily pre-treated, refractory patients with lymphoproliferative disorders. Half of the patients in this small study responded although responses were usually brief. Importantly, one patient with compromised renal function was treated successfully with this single drug program and has been in remission for longer than one year. Two of these patients with CNS lymphoma, refractory to steroids and radiotherapy, also responded. Sustained remissions and complete remissions may have been compromised by systemic relapse that occurred in each case after an initial response. Toxicity has been obviated by the

use of CF rescue and alkalinization of urine with sodium bicarbonate which minimizes precipitation of the drug in the renal tubules and promotes excretion.¹⁸ Although the dose of 250mg./m² used in this paper produced objective responses, a higher percentage of remissions and more durable responses have been achieved using doses of 1-3gm./m².²² In addition, therapy in that series was given weekly rather than bi-monthly.

The rationale for employing HD-MTX/CF in this study is based upon several factors: A higher therapeutic ratio may be achieved in some malignancies compared to conventional dose MTX. Standard doses of MTX in lymphomas produce a response rate at only 29%,²⁴ lower than the 50% achieved in this study and much lower than 80% achieved in a study with even higher doses.²² The pharmacologic mechanisms involved in this approach to chemotherapy involve differences between carrier-mediated cell membrane transport systems of tumor cells versus normal marrow cells.²⁵ CF may selectively rescue normal cells rather than tumor tissue. Recent work demonstrates that MTX, although it primarily inhibits thymidylate synthesis, may also inhibit purine biosynthesis.²⁵ Rapidly growing malignancies with a high growth fraction, such as diffuse histiocytic lymphoma, may be particularly sensitive to HD-MTX/CF. However, the duration of remission may be short particularly when HD-MTX/CF is used alone. This was observed in the present study; responses were rapid but brief. Achievement of therapeutic levels of MTX in the CNS after systemic administration of high doses in this study as well as others²² suggests a possible role in the prophylaxis of CNS disease. CSF levels of MTX should have been determined in the present study. Although two of the three patients responded with a reduction in the CSF protein and cell count, it would have been helpful to document whether a therapeutic level was achieved in the patients who failed to respond or whether there was drug resistance. In patients with non-Hodgkin's lymphoma with unfavorable histologies, 25-30% of patients develop CNS disease.²⁶ HD-MTX/CF may be as effective as irradiation, corticosteroids and intrathecal chemotherapy. This is suggested in the present study but is more impressive in a study using higher doses resulting in higher CSF levels.²² In addition, the majority of patients have or will develop accompanying systemic disease which can respond to HD-MTX/CF. In the present study, remissions occurred in all areas of involvement including the CNS. In one patient whose CNS disease did not respond, systemic disease also did not respond.

Use of HD-MTX/CF as a single agent in advanced disease refractory to conventional agents, produces limited responses, which are generally short lived. However, the results suggest a possible role for HD-MTX/CF combined with other active agents in newly diagnosed patients particularly with non-Hodgkin's lymphoma. The purposes would be to add an additional effective drug that does not have myelosup-

pressive toxicity to the regimen and to reduce the occurrence of CNS lymphoma. Such a study is now in progress and has shown both high systemic remission rates and low CNS recurrence.²⁷

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Arterial Graft Infection and Aortic Fistulae

Maine Medical Experience 1974-1979

IRVING KRON, M.D.* AND FERRIS RAY, M.D.*

Vascular graft infection is a highly lethal complication of arterial reconstructive surgery. Proximal aortic suture line involvement, including aorto-duodenal fistula, carries a mortality rate of between 75% and 100%.^{1,2} The incidence of this complication in most reported series is between 1% and 2%.³ Several recent cases referred to our institution with graft infection led us to review our recent experience. For the purpose of our review, we made the assumption that aortoenteric fistula implied graft infection.

CLINICAL MATERIAL

All cases of arterial graft infection, including aortoenteric fistulae, treated at the Maine Medical Center between 1974 and 1979 were chosen for review. There were a total of eleven infections involving aortic grafts, nine of which presented as enteric fistulae. There were six cases involving femoral grafts.

RESULTS

The mortality in our series was 73% for aortic graft involvement and 17% for femoral graft infection. Several procedures were performed attempting to treat these problems, particularly at the aortic level (Table 1). The only excellent result involved local repair with saphenous vein patch graft and systemic antibiotics which is described in a previous publication.⁴ The results of this procedure in two other patients were not so successful. One patient died of recurrent fistula with hemorrhage. Another patient's fistula recurred three years postoperatively and was repatched. She subsequently lost a limb to progressive atherosclerotic disease one year following the second fistula repair.

No other method of treatment had any more encouraging results. One patient had fistula exclusion as a lifesaving maneuver.⁵ He succumbed to recurrent graft fistula and sepsis two years later. Only one patient had graft excision and extra-anatomic bypass, but he died intraoperatively. No statement can be made about the long-term results of this procedure from our series.

The results of procedures for femoral graft sepsis were somewhat better (Table 2). Graft removal with or without alternate bypass had good results in two out of three cases. Local repair resulted in one death from hemorrhage and sepsis as well as two local complications. Three of these patients including the one who died had saphenous vein used as the original graft material.

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TABLE 1

RESULTS OF PROCEDURES FOR AORTIC GRAFT INFECTION OR FISTULA					
Procedure	# Of Patients	Dead	Limb Loss	Good Result	Survivors
None	2	2			0
Graft Excision & Alternate Bypass	1	1*			0
Local Repair	3	1	1**	1	2
Regraft	4	3	1		1
Fistula Excision	1	1***			0
Totals	11	8 (73%)	2	1	3

*Intraoperative Death

**Also had Recurrent Fistula

***Died 2 Years Postoperative—Recurrent Fistula and Sepsis

TABLE 2

RESULTS OF PROCEDURE FOR FEMORAL GRAFT SEPSIS				
Procedure	# Of Patients	Dead	Limb Loss	Good Result
Removal Graft	2		1	1
Graft Excision & Alternate Bypass	1			1
Local Repair	3*	1		
Totals	6	1 (17%)	1 (17%)	2 (33%)

*With False Aneurysm

Other with Small Draining Sinus

In our series, the interval between the original aortic procedure and the development of signs of infection or fistula was between one month and ten years with an average of 5.2 years. Femoral graft sepsis manifested itself more acutely with an interval of ten days to five years. This may have been a function of the bacterial organism involved. *Staphylococcus Aureus* predominated in the femoral graft group as opposed to coliforms in the aortic group.

A major problem was the diagnosis of aortoenteric fistula. There was an average duration of eight months of symptoms prior to the correct diagnosis; the most common of these were lower gastrointestinal bleeding and anemia (Table 3). Barium studies and radionuclide gallium scans were not of value in our series. Angiography was diagnostic in one case where a false aneurysm was

TABLE 3

**AORTOENTERIC FISTULA—CASES
DURATION OF SYMPTOMS PRIOR TO DIAGNOSIS**

1 DAY—3 YEARS (AVG. 8 MOS.)

SIGNS AND SYMPTOMS

Anemia	5
Abdominal Pain	2
Weight Loss	2
G I Bleed	9
Septic Emboli	1

present. Endoscopy was helpful in excluding other lesions but was misleading on three occasions. In these cases gastritis, duodenitis, and cecal angiodysplasia were thought to be the sources of bleeding.

DISCUSSION

The mortality of our series for aortic graft sepsis and fistulae is consistent with most other reported series. The major problems seemed to be failure of early recognition and inadequate surgical therapy in this critically ill group of patients.

The diagnosis of aortoenteric fistula is made on clinical grounds.⁶ Angiography and barium studies are helpful only if positive. Endoscopy may be useful to exclude other lesions. In one major reported series of nineteen aortoenteric fistulae, the diagnosis was made preoperatively only twice.⁷ Early laparotomy is the most effective means of diagnosis if this condition cannot be excluded by other methods.

One reason for conservative repair of aortoduodenal fistula is the feeling that this may not represent a septic process. Recent data suggests, however, that low grade suture line infection is the primary etiology of aortoduodenal fistula.⁸ A collective review demonstrated that local repair of aortoduodenal fistula had an 87% mortality as compared to a 13% mortality with graft excision and alternate conduit.⁹ Our experience suggests that a more aggressive approach both diagnostically and therapeutically may improve survival.

Our results with femoral graft sepsis were somewhat better. Local drainage and repair in the

groin usually resulted in complications. However, it has been suggested that prompt local treatment of acute groin sepsis may be successful.¹⁰

In our series, 50% of the infected femoral grafts involved saphenous vein grafts. The only death in this subgroup involved sepsis and hemorrhage in a saphenous vein femoral to popliteal graft. The saphenous vein graft is not immune to infection and actually has a higher hemorrhage rate than dacron.¹¹

SUMMARY

Early diagnosis and aggressive surgery are the only ways to reduce the excessive mortality of arterial graft infection. Diagnosis usually requires early surgical exploration. Therapy usually requires graft excision and alternate bypass except in very unusual circumstances. The basic problem in the aortoenteric fistula seems to be unrecognized underlying sepsis which results in fistula recurrence and other septic complications if only locally repaired.

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Blunt Mesenteric Vein Trauma

IRVING KRON, M.D.* AND JAMES GEORGITIS, M.D.*

Less than 0.2% of non-penetrating abdominal trauma results in injury to the mesenteric vessels.¹ Stone reported that superior mesenteric vein injury was associated with a 50% mortality, portal vein injury with a 71% mortality,² and both with a 100% mortality. Graham, Mattox, and Beall reported 68.8% survival after superior mesenteric injury and 48.7% after portal vein injury.³

The reported high mortality of blunt disruptive injuries of the superior mesenteric vein appears to be related to the paucity of clinical experience in the

mesenteric vein tears, at the root of the mesentery was isolated, bleeding controlled by digital pressure during dissection to expose the extent of truncal injury, and repair accomplished by over and over continuous suture of 5-0 prolene. No local or systemic anticoagulation was used. Mesenteric vein truncal injuries were as depicted in Figure 1.

COMPLICATIONS

There were no complications related to the mesenteric vein injury per se. Case 1 developed a

TABLE 1

	Case 1	Case 2	Case 3	Case 4
AGE	34	41	53	17
ASSOC. INJURIES	splenic capsular tear contused pancreas	fracture of radius & ulna	fractures lt ribs 6-8; splenic capsule tear torn mesentery	closed head injury torn mesentery
TIME SINCE INJURY	2 hrs	1 hr	2 hrs	3 hrs
BP ON ADMISSION	*80/60	*80/60	*70/40	*90/50

*arm pressures

management of this uncommon type of injury. Recent experience with four patients sustaining this injury without mortality prompts this report of the details of management and a review of the literature.

CLINICAL MATERIAL

Four males ranging in age from 17 to 53 years sustained deceleration trauma in vehicular accidents during which none wore a seat belt. They were received in the Maine Medical Center Emergency Room from one to three hours following injury. All were hypotensive but responded to volume resuscitation with 1500 to 3000 ml of crystalloid intravenously. Gross associated injuries included closed fractures of the forearm in Case 2, fractures of left ribs 6-8 in Case 3, and closed head injury in Case 4.^{2,6-8} Physical findings in the three conscious patients included mild epigastric tenderness to palpation, hypoactive bowel sounds, and no cutaneous abrasions or ecchymoses. Peritoneal lavage was positive for gross blood in all four. Following radiological assessment of the skeleton and intravenous pyelography, operations were performed (Table 1).

After evacuation of blood and clots through midline exploratory incisions, the area of superior

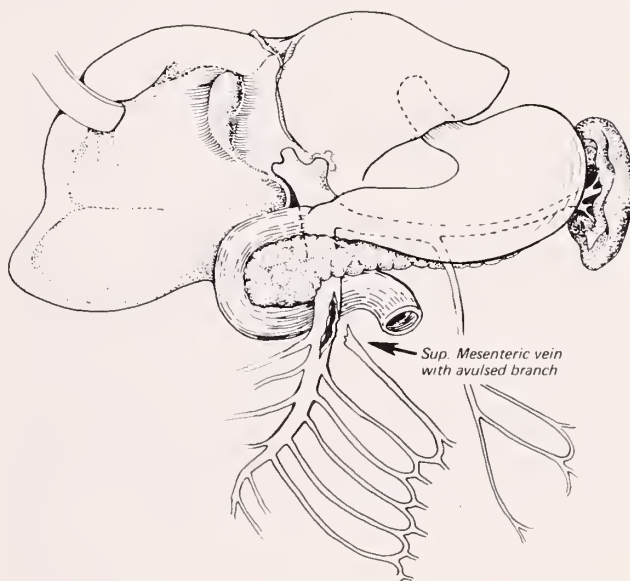


Fig. 1

postoperative pancreatic fistula related to traumatic contusion of the pancreas.

DISCUSSION

Trauma to mesenteric veins presents a problem because of massive hemorrhage from low pressure—high flow vessels. Isolated blunt traumatic injuries of

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the superior mesenteric vein are uncommon. A recent large series discussed only 45 superior mesenteric venous injuries collected over a 13-year period, very few of which were secondary to blunt trauma.⁴ We have encountered four superior mesenteric vein injuries due to blunt trauma over the last two years. All injuries were suffered by automobile passengers not wearing seat belts. Each patient entered the emergency room mildly hypotensive with an average systolic pressure of 80 mm. of mercury. Each of the venous tears was repaired by lateral venorrhaphy. An average of four and a half units of blood were required for stabilization. All patients survived and the only morbidity was that of a pancreatic fistula which closed spontaneously on the 57th day.

Injuries to the superior mesenteric vein from blunt trauma appear as lateral rents in the vessel, presumably as a result of deceleration creating shear at the lateral venous branch junctions and leading to disruption (Figure 1). Avulsion with linear defects occurs because of lesser tensile strength of the vein wall. The tethering of the mesenteric vein at the root of the mesentery creates a point of fixation which is prone to injury as the mesentery swings in pendulum fashion.

Injuries to the superior mesenteric vein have been reported to have a mortality of 70 percent in a series predominantly related to penetrating trauma.⁵ The 100% survival in our series reflects the more benign nature of isolated blunt venous injury and early vessel repair. Our patients were not severely hypotensive when first seen, probably due to the tamponading effect of overlying bowel. Associated injuries were few and of non-lethal type as compared with other series.⁶

Lateral venorrhaphy was the method of repair used in each case. After quickly inspecting the liver and spleen for major injuries, the bleeding from the mesenteric vein tear was controlled by digital pressure. Without use of anticoagulants the injury was repaired anatomically. No postoperative anticoagulation was utilized. Other methods reported in the literature include end-to-end anastomosis, simple ligation, and use of interposition grafts.^{5,6,7,8} Simple ligation has been used successfully in some cases but has also been associated with small bowel infarction and subsequent death.^{3,6,7,8} The few cases reported having successful mesenteric vein ligations have been for elective tumor resection.⁷ The low flow state caused by severe trauma may be a further contraindi-

cation to the use of ligation for mesenteric vein injury.

SUMMARY

Superior mesenteric vein injury resulting from blunt trauma is unusual. This type of injury has a significantly better prognosis than injury resulting from penetrating trauma since it is less frequently associated with concurrent lethal organ damage. Anatomic repair is the choice of surgical control as opposed to simple ligation which may lead to mesenteric thrombosis and death.

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Sleep Apnea Syndromes

GEORGE E. BOKINSKY, M.D.*, WILLIAM MAXWELL, M.D.**
AND PAUL M. COX, JR., M.D.***

INTRODUCTION

During the past 15 years, studies have demonstrated the frequent occurrence in certain patients of abnormal breathing during sleep. These patients intermittently stop breathing during sleep, leading to (1) frequent arousal and sleep deprivation and (2) repetitive hypoxemia with acidemia. As a result of these studies, previously diverse conditions such as the Pickwickian syndrome, obesity with hypersomnia, Ondine's curse, and various forms of narcolepsy are now recognized as manifestations of the broad category of sleep apnea syndrome. With an understanding of pathophysiology, effective treatment has become available. This report describes three patients seen at the Maine Medical Center with sleep apnea syndrome.

CASE SUMMARIES

Case 1: A 33-year-old male was admitted to the Maine Medical Center in 1975 because of respiratory failure. As a child, he contracted pneumonia and following this illness experienced recurrent episodes of bronchitis into adult life. In the 12 years preceding admission, he noted progressive weight gain from 147 to 288 pounds, and during this period began to experience daytime hypersomnia, manifest by falling asleep while driving a truck, personality change with marked irritability, and early morning bifrontal headaches. Abnormal nighttime sleep was not described.

On admission to hospital, he was an obese male, cyanotic with marked peripheral lower extremity edema. His cardiac and respiratory failure responded to aggressive treatment, including a brief period of assisted ventilation. Following extubation, the staff noted repetitive episodes of apnea during sleep in spite of increased respiratory efforts. These apneic episodes would terminate with a loud snoring sound.

Efforts to establish a patent airway by position change and by use of a soft, nasopharyngeal airway were ineffective. A tracheostomy was created to correct the intermittent upper airway obstruction. Following tracheostomy, the patient slept soundly for 48 hours. With a functioning tracheostomy, he has experienced no subsequent hypersomnia, abnormal irritability, early morning headaches, or heart failure in the past five years.

Case 2: A 30-year-old male sought medical attention because of severe headaches. Complete neurological and psychiatric examinations were unsuccessful in establishing either a diagnosis or effective therapy. He had been gainfully employed as a draftsman, but these symptoms led to impairment of concentration that caused him to lose his job. Following an automobile accident resulting from falling asleep while at the wheel, an abnormal sleep history was obtained consisting of daytime hypersomnia, nocturnal insomnia, and while asleep, frequent episodes of apnea accompanied by stertorous breathing, terminated by loud snoring. Enuresis and

impotence were later described. He was undergoing treatment for systemic arterial hypertension.

Physical examination revealed an obese (mass 114 kg) and hypertensive male. There is no evidence for obstruction of his upper airway, or congestive heart failure, and all laboratory investigations were normal.

Sleep studies were performed after overnight sleep deprivation with continuous recordings of arterial oxygen saturation by air oximetry, intrathoracic pressure by esophageal manometry, end-tidal partial pressure of carbon dioxide at the nose and mouth using a mass spectrograph and electroencephalogram to document sleep stage. These studies documented frequent obstructive apneas manifest by cessation of air flow in spite of increased ventilatory effort. Apneas occurred with a frequency of 128 per hour with an average duration of 24-30 seconds. Accompanying these apneas, were repetitive oxygen desaturations to as low as 58%, corresponding to an arterial oxygen tension of 35 torr. During the recording, no episodes of rapid eye movement sleep were observed, and sleep was equally divided between stages I and II, non-rapid eye movement sleep with frequent arousal.

Attempts at weight loss and use of a soft nasopharyngeal airway were ineffective in correcting these apneas. A permanent tracheostomy was created that could be capped and covered during the daytime hours, permitting normal speech. Following this complete resolution of the obstructive apneas with reestablishment of a normal nocturnal sleep pattern without daytime hypersomnia occurred. Enuresis and impotence resolved. His arterial blood pressure became normal and no longer required anti-hypertensive agents.

Case 3: A 15-year-old male was noted by his mother to have abnormal nighttime sleep, highlighted by violent movements of arms and legs, as well as nightly enuresis. Daytime hypersomnia while at school, during conversation, and even during meals was noted in spite of nighttime sleep of approximately 12 hours. Loud and pharyngeal snoring was noted throughout the night, often keeping his mother awake. Poor school performance and constant fatigue were alarming to the patient's parents. His past medical history revealed that a nasal septoplasty, as well as tonsillectomy and adenoidectomy were performed in an attempt to provide a more patent upper airway. A seizure disorder was present from age 9 months to age 5 years, and mild mental retardation was present.

Examination revealed a tall, thin normotensive male with frontal bossing, micrognathia, and nasal obstruction. The remainder of the physical examination was unremarkable. A 24-hour dynamic electrocardiogram showed frequent periods of sinus arrhythmia and wandering atrial pacemaker with isolated ventricular premature beats.

Sleep was studied in the fashion described for Case 2. Eighty-six episodes of desaturation were observed over 83 minutes, with the lowest saturation of 44%. Most episodes of desaturation were to between 70% and 80%. All apneas were obstructive with durations between 30 and 60 seconds. While breathing quietly, minimal abdominal motions were noted, progressing to marked respiratory efforts with paradoxical anterior chest wall motion. These episodes of apnea were terminated by three to four loud pharyngeal snores.

Obstructive sleep apnea was demonstrated, and in an attempt to avoid tracheostomy, he was briefly tried on Methylprogesterone, 10 mg every eight hours, without success. Tracheostomy was followed by a return to a normal sleep pattern, disappearance of daytime hypersomnia and enuresis, and an improvement in school performance.

DISCUSSION

The sleep apnea syndromes are classified into obstructive or nonobstructive categories (Table 1).

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TABLE 1

Predominately Obstructive

1. Obesity with hypersomnia
2. Pickwickian syndrome
3. Primary sleep apnea
4. REM narcolepsy
5. Hypersomnia

Predominately Central

1. Ondine's curse
2. Insomnia
3. Sudden infant death syndrome
4. With known neural disease
 - (a) Postencephalitis
 - (b) Polio
 - (c) Bilateral cervical cordotomy

To an extent, a degree of overlap exists so that a patient with sleep apnea syndrome may show apneas of both types. Most patients will have a normal upper airway, and a minority will show an anatomical defect such as micrognathia, laryngeal stenosis, or enlarged tonsils and adenoids.^{1,2} Certain patients with chronic bronchitis and emphysema may also show disordered breathing and oxygen desaturation during sleep.^{3,4} There is also evidence for obstructive sleep apnea on a familial basis.⁵ To understand the events occurring in the sleep apnea syndrome, an understanding of the structure of normal sleep, as well as its hemodynamic and respiratory changes is necessary.^{6,7,8} By electroencephalographic criteria, sleep is classified as non-rapid eye movement sleep and rapid eye movement sleep. There are four levels of non-REM sleep, representing deeper levels of sleep. While deeper levels of non-REM sleep are fairly quiet, and apneas of greater than 15 seconds duration are rare in normal subjects, REM sleep is accompanied by increased physiological activity and apneas of more than 15 seconds duration may be observed.⁹ With the exception of REM sleep and early sleep, normal subjects show a regular respiratory rhythm, rare apneas, mild hypoventilation, and a hemodynamic profile of regularity in cardiac rhythm and a decline in arterial blood pressure.

A variety of mechanisms have been proposed to explain the obstruction that occurs in sleep apnea syndrome. Cineradiographic and direct fiberoptic observations have shown the obstruction to occur at the oropharyngeal-nasopharyngeal junction. Borowiecki, et al,¹⁰ using these techniques demonstrated the velopharyngeal sphincter and tongue to be the structures involved in the production of airway obstruction. The obstructive phenomenon begins during late expiration and continues throughout the inspiratory cycle with the tongue projected upward and posterior, thus closing the oral airway. The role of the tongue was further investigated by Remmers, et al,¹¹ using genioglossus electromyographic recordings in a series of 10 patients with daytime hypersomnolence and obesity. The genioglossus EMG revealed periodicity with a low level of activity at onset of occlusion and prominent activity at the instant of pharyngeal opening. Thus, it appears that

active contraction of the genioglossus muscle is necessary to maintain oropharyngeal patency at least during the inspiratory phase.

It should be emphasized that a spectrum of involvement exists, ranging from loud snoring and hypoventilation as a consequence of partial obstruction of the upper airway during sleep to apnea with severe ventilatory and cardiovascular consequences following complete obstruction. Those patients within the obstructive apnea category have literally hundreds of apneas during an eight-hour sleep cycle, with durations of 20-30 seconds per apnea. Based on the observations of Guilleminault,¹ patients with the Pickwickian syndrome, obesity with sleep apnea, and nonobese obstructive sleep apnea cannot be distinguished on the basis of a number or duration of apneas during sleep. In contrast to patients with obstructive sleep apnea, those with central apneas have fewer apneas, but each apnea is of a longer duration.

Sleep apnea may produce serious hemodynamic consequences as a result of the hypoxemia and respiratory acidosis.^{12,13} Arrhythmias, conduction disturbances, and extreme sinus bradycardia have been reported with sufficient frequency to recommend overnight electrocardiographic monitoring as a screening procedure.¹² Severe and sustained elevations of pulmonary artery and systemic arterial pressures have been recorded.¹² Over the course of years, these patients then become a risk for sudden death because of arrhythmias or cerebral vascular accidents related to this mechanism or severe elevations of blood pressure during sleep. The sustained pulmonary artery hypertension leads eventually to cor pulmonale.

The patients with sleep apnea syndrome experience a variety of symptoms that may eventually lead to medical attention. These symptoms are frequently nonspecific and commonly related by patients who do not have the sleep apnea syndrome. It is the association of these complaints with a history of abnormal sleep that frequently must be elicited from the patient's family that allow a tentative diagnosis of a sleep apnea syndrome. All studies have shown a strong male predominance.¹⁴ Symptoms are also chronic and many may note these complaints for more than ten years before a diagnosis is made.

The symptoms, as seen in Table 2, suggest neurological, psychiatric, or sleep-related disorders. Examination while awake is usually normal. No abnormalities of the upper airway can be detected while awake. While only a small percentage is typically Pickwickian, the majority are obese.^{14,15} Essential hypertension is present in approximately 60%.¹

Confirmation of the diagnosis should involve physiologic studies confirming that (1) the patient is asleep, (2) that apnea occurs, (3) that apneas are obstructive, nonobstructive or both, and (4) that severe hypoxemia occurs as a consequence. The studies of Block, et al,⁹ make it clear that desaturation and apnea are seen in normal male subjects with a frequency increasing with increasing weight. It is

TABLE 2

Neuro-Psychiatric Symptoms

1. Early morning headaches
2. Depression, irritability
3. Chronic fatigue
4. Impaired concentration—in up to 60%
5. Impotence—in 48%
6. Enuresis—most children, 8% of adults

Sleep-Related Symptoms

1. Insomnia
2. Abnormally long nocturnal sleep
3. Daytime hypersomnia, narcolepsy in up to 90%
4. Restless leg syndrome, nocturnal myoclonus
5. Violent hand-arm movements
6. Somnambulism
7. Difficulty arousing patient from sleep
8. Temporal, spatial disorientation on arousal
9. Apneas and loud-pharyngeal snoring

crucial that this normal phenomenon be separated from the syndrome of sleep apnea. Accurate documentation of the frequency and duration of apnea, as well as the degree of desaturation, are crucial means of making this distinction.

The capability of continuously monitoring and recording the variables of arterial saturation, respiratory muscle activity, air flow, and sleep stage greatly facilitates making the diagnosis.

Treatment should be viewed against the background of the natural history of this disorder. While sleep apnea syndrome is a chronic disorder, the mortality in the Pickwickian patients who show right ventricular failure is extremely high,¹⁶⁻¹⁷ and sudden deaths have been reported in nonobese patients with the sleep apnea syndrome as well.⁵ Attempts to relieve the intermittent obstruction by sleeping in a prone position and by use of a nasopharyngeal airway have been both ineffective and poorly tolerated. The use of progestational agents has been suggested by its effectiveness in the full-blown Pickwickian syndrome,¹⁷ as well as by the observed rarity of sleep apnea syndrome in women. The role of such agents is unproven at this time.

Tracheostomy has produced dramatic improvement in both symptoms and observed physiologic derangements. Benefit is almost immediate, and where studied, abolition of the obstructive apneas with desaturation, correction of both pulmonary and systemic hypertension, and relief of arrhythmias have occurred.¹⁸ For the small group of patients with central, nonobstructive apneas, phrenic nerve pacing has occasionally helped.¹⁹

While abnormal breathing during sleep is common in many men,⁹ the sleep apnea syndrome is not. It is important to recognize that a spectrum of involvement exists, ranging from loud snoring during sleep to the end stage Pickwickian syndrome. Within this

spectrum there are many patients whose nonspecific symptoms may be caused by sleep apnea and who can obtain benefit by effective treatment.²⁰

ACKNOWLEDGMENTS

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What, Where, How...and Why HLA?

PAULA J. ROMANO, PH.D.*

Recent discoveries in the area of immunogenetics are having an increasing impact on clinical medicine. Immunogenetics? "Self vs. nonself"—that exquisite sensing mechanism that triggers off a cascade of genetically controlled immune responses to foreignness, as well as the transmission of antigenic specificities from generation to generation.

Genetic influences control the maturation of immune mechanisms within the individual. Genetic factors operate at a cellular level, as the proliferation and differentiation of a variety of cell types in response to antigen. At the molecular level, unlimited variability occurs in immunoglobulin structures that are directly encoded into DNA. Finally, information for antigens themselves, such as blood group and histocompatibility (HLA) antigens, are also transmitted genetically. Moreover, closely related to the HLA loci are genes which actually control and/or influence immune responsiveness.

The human histocompatibility antigens represent the most polymorphic antigen system known in man. What biological advantage can be credited with maintenance of such multiple antigenic determinants? It is well known that HLA antigens play a major role in cell and organ transplantation. However, these are not naturally occurring phenomena, hence unlikely mechanisms for selective pressure. The more fascinating explanation for the existence of this highly variable genetic system implies a fundamental biologic process—immune responsiveness.

A wide range of diseases has been studied in which certain of these histocompatibility antigens have appeared in greater frequency than would be expected in the normal random population. This relationship of HLA with disease has its basis in studies of inbred strains of mice. Immune response (IR) genes controlling reactively to about 20 different antigens, have been found to be linked to genes coding for mouse histocompatibility antigens. The human HLA-DRw antigens appear to be analogs of these mouse antigens, and likewise may identify or be associated with human immune response genes. This article will provide an introduction to this rapidly moving field and offer a brief commentary on the implications of these new developments.

HISTORY

The discovery by Jean Dausset in 1954, that leucopenic and hypoplastic patients often developed antibodies to white blood cells, led to the identification of the major histocompatibility complex (MHC) of man.¹ Brittingham soon demonstrated leuco-

agglutinating antibodies associated with febrile, non-hemolytic transfusion reactions.² In 1958, Rose Payne found that the sera of multiparous women also contained some of these same antibodies.³ Studies in mice, and subsequently in humans, showed that these antibodies were directed against antigens which could cause accelerated rejection of skin grafts.^{4,5} This expression of leucocyte antigens on other tissues suggested the importance of their role in cell and organ transplantation.

The identification of HLA antigens progressed rapidly as a variety of new and improved techniques were introduced. In particular, the miniaturization of the cytotoxicity assay by Terasaki allowed as many as 1000 test determinations to be made with 1 ml. of antiserum.⁶ Analysis of serological results was made by comparing all the reaction patterns of cell donors, although characterization of antigens were difficult due to the multispecific nature of the majority of antisera. Van Rood clarified the problem by application of computer analysis techniques and testing sera against a panel of 100 cells from random donors.⁷ Moreover, the establishment in 1964 of periodic workshops, gathering together groups of international investigators, has promoted an invaluable exchange of information. The biological significance of the HLA complex has been extended far beyond the area of transplantation to involve an association with a variety of diseases and linkage with a number of immunologically mediated cell surface recognition events.

GENETICS OF HLA

The human MHC is located on chromosome 6 and is composed of four major genetic units, the HLA-A, -B, -C, and -D/DR loci (Figure 1). Since the MHC gene products of both chromosomes are both expressed (codominance), each individual may possess a total of eight HLA antigens. In practice, the full complement of eight antigens is seldom found for several reasons including: homozygosity at a given locus (i.e. identical genes), deletion of genetic material at a locus, and/or lack of more precise antisera as testing reagents.

The four HLA gene products derived from one chromosome is called a haplotype (Figure 2). The tissue type of a family, in which the antigens of each individual are segregated into the two haplotypes is called a genotype. The tissue type of an individual, which simply identifies the eight antigens, is a phenotype. Family studies have shown that recombination does occur between each of the HLA-A, -B, -C, and -D loci, demonstrating that they are separate genetic events. A given set of parents can produce offspring with only four possible combinations of haplotypes (unless a crossover has occurred). Thus,

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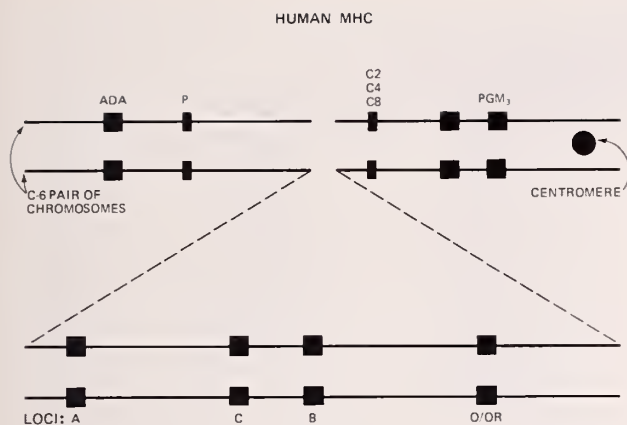


Fig. 1

there is a 1:4 probability of two offspring being HLA-identical. Moreover, a parent and child can share only one haplotype unless both parents possess antigens in common. HLA identity (histocompatibility) between siblings actually represents identity of the entire HLA genetic region: those MHC components which we can identify by current techniques and those determinants which are still indiscernable. On the other hand, HLA "identity" between two unrelated individuals refers only to those gene products which we know exist and for which we have an assay system available.

The genes associated with these four loci show three important characteristics: 1) each locus represents an allelic system with considerable polymorphism (Table 1), 2) the determinants of each locus demonstrate cross-reactivity, and 3) genetic linkage disequilibrium exists among the alleles of the different loci, e.g., some combinations of antigens on haplotypes (A1, B8; A2, B12; A3, B7) are more common than would be expected by random association. This phenomenon may be explained by genes of the HLA region being held in biologically desirable combinations by natural selection.

TISSUE AND CELL DISTRIBUTION

The presence of an antigen on a cell surface can be determined by direct testing of the cells with appropriate antisera (cytotoxicity, agglutination, fluorescence) or indirectly, by assaying the ability of these cells to absorb out a particular antigenic activity from an antiserum (absorption).

Using both types of testing, HLA antigens have been demonstrated on a variety of cells and tissues, although in varying concentrations. White blood cells were found to have the largest absorptive capacity,⁸ although the concentration of HLA antigens on lymphocytes is reported to be greater than that on granulocytes⁹ or platelets.¹⁰ Cultured human lymphocytes provide an increase of 20 to 40 fold the amount of antigen found on normal peripheral lymphocytes,¹¹ yet on a per-unit-area basis, platelets reportedly possess more antigen than lymphoblastoid cells.¹² HLA antigens are not detectable on mature erythrocytes, although they have been reported on

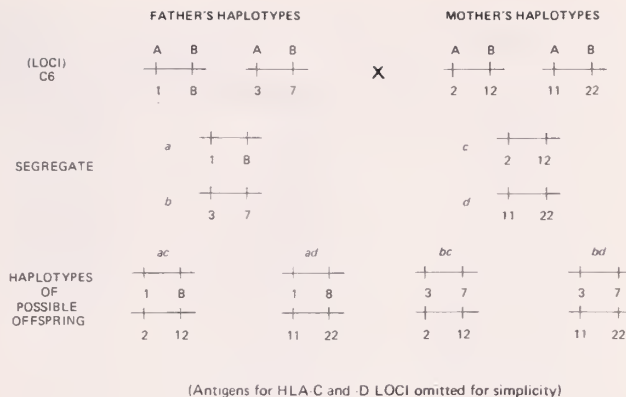


Fig. 2

their nucleated erythrocyte precursors.¹³ Moreover, saliva, serum, and colostrum also contain HLA antigens, although in soluble form.¹⁴ Using absorption techniques to study the organ distribution of HLA A-2, spleen was found to be the richest, followed by lung, liver, intestine, kidney, and heart, with practically none present on fat or brain tissue.¹⁵ Moreover, HLA antigens are also present on spermatozoa,¹⁶ placenta (at term¹⁷) and the developing embryo, although absent from the trophoblast.¹⁸

The distribution of HLA antigens among the cells involved in an immune response is further restricted. HLA-A, -B, and -C antigens are generally found on all cells (T lymphocytes, B lymphocytes, monocytes, etc.) whereas HLA-D antigens are limited to B lymphocytes and monocytes.¹⁹ Moreover, discrepancies occur in detection of HLA-D depending upon whether the antigens are studied by serological (DR typing) or cellular (D typing: mixed lymphocyte culture) techniques.

SOURCE OF HLA ANTIBODIES

The occurrence of antibodies to HLA antigens, in the general population, is usually very rare unless an individual has been previously sensitized. Since histocompatibility antigens are ubiquitous in their distribution, immunization may occur in various ways following presentation of allogeneic antigens. Skin grafting,²⁰ blood transfusion,²¹ planned immunization²² and pregnancy^{23,24} may all induce antibody formation. Repeated exposure is usually necessary, although route of administration, type and amount of tissue or cell, interval between sensitizations and presence of preformed antibody all influence the response.

Nevertheless, the most abundant source of anti-HLA antibodies is provided by sera from multiparous women. Quality control, standardization, and sera exchanged among investigators, is carefully maintained by the coordinating efforts of the National Institutes of Health (NIH) Serum Bank in Bethesda, Maryland.

BIOCHEMISTRY OF HLA

A complete understanding of the biological roles

TABLE 1

COMPLETE LISTING OF RECOGNIZED HLA SPECIFICITIES

HLA-A	HLA-B	HLA-C	HLA-D	HLA-DR
HLA-A1	HLA-B5	HLA-Cw1	HLA-Dw1	HLA-DR1
HLA-A2	HLA-B7	HLA-Cw2	HLA-Dw2	HLA-DR2
HLA-A3	HLA-B8	HLA-Cw3	HLA-Dw3	HLA-DR3
HLA-A9	HLA-B12	HLA-Cw4	HLA-Dw4	HLA-DR4
HLA-A10	HLA-B13	HLA-Cw5	HLA-Dw5	HLA-DR5
HLA-A11	HLA-B14	HLA-Cw5	HLA-Dw6	HLA-DRw6
HLA-Aw19	HLA-B15	HLA-Cw7	HLA-Dw7	HLA-DR7
HLA-Aw23(9)	HLA-Bw16	HLA-Cw8	HLA-Dw8	HLA-DRw8
HLA-Aw24(9)	HLA-B17		HLA-Dw9	HLA-DRw9
HLA-A25(10)	HLA-B18		HLA-Dw10	HLA-DRw10
HLA-A26(10)	HLA-Bw21		HLA-Dw11	
HLA-A28	HLA-Bw22		HLA-Dw12	
HLA-A29	HLA-B27			
HLA-Aw30	HLA-Bw35			
HLA-Aw31	HLA-B37			
HLA-Aw32	HLA-Bw38(w16)			
HLA-Aw33	HLA-Bw39(w16)			
HLA-Aw34	HLA-B40			
HLA-Aw36	HLA-Bw41			
HLA-Aw43	HLA-Bw42			
	HLA-Bw44(12)			
	HLA-Bw45(12)			
	HLA-Bw46			
	HLA-Bw47			
	HLA-Bw48			
	HLA-Bw49(w21)			
	HLA-Bw50(w21)			
	HLA-Bw51(5)			
	HLA-Bw52(5)			
	HLA-Bw53			
	HLA-Bw54(w22)			
	HLA-Bw55(w22)			
	HLA-Bw56(w22)			
	HLA-Bw57(17)			
	HLA-Bw58(17)			
	HLA-Bw59			
	HLA-Bw60(40)			
	HLA-Bw61(40)			
	HLA-Bw62(15)			
	HLA-Bw63(15)			
	HLA-Bw4 ^a			
	HLA-Bw6			

The listing of broad specificities in parentheses after a narrow specificity, e.g., HLA-Aw23(9) is optional. The following is a listing of these specificities which arose as clear-cut splits of other specificities.

<i>Original broad specificity</i>	<i>Splits</i>
HLA-A9	Aw23, Aw24
HLA-A10	A25, A26
HLA-B5	Bw51, Bw52
HLA-B12	Bw44, Bw45
HLA-B15	Bw62, Bw63
HLA-Bw16	Bw38, Bw39
HLA-B17	Bw57, Bw58
HLA-Bw21	Bw49, Bw50
HLA-Bw22	Bw54, Bw55, Bw56
HLA-B40	Bw60, Bw61

^aThe following are the generally agreed inclusions of HLA-B specificities into Bw4 and Bw6.

Bw4:	B13, B27, B37, Bw38(w16), Bw44(12), Bw47, Bw49(w21), Bw51(5), Bw52(5), Bw53, Bw57(17), Bw58(17), Bw59, Bw63(15)
Bw6:	B7, B8, B14, B18, Bw35, Bw39(16), Bw41, Bw42, Bw45(12), Bw46, Bw48, Bw50(w21), Bw54(w22), Bw55(w22), Bw56(w22), Bw60(40), Bw61(40), Bw62(15).

of the HLA-A, -B, -C, and -D/DR antigens depends ultimately upon a detailed knowledge of their molecular configuration. It is crucial to establish whether the gene products are structurally related, as structural homology implies that the gene products mediate similar functions. Indeed, the antigens of the

HLA-A, -B, and -C loci possess similar biochemical structures.²⁵ These molecules are composed of a glycosylated polypeptide chain of about 43,000 molecular weight, that is non-covalently associated with a smaller, non-glycosylated polypeptide of about 12,000 molecular weight, identical to B₂-

microglobulin. This HLA associated B₂-m is completely cross-reactive with that isolated from urine; however, it does not contribute to the polymorphism of the HLA antigens. This antigenic activity appears to be determined exclusively by the 43,000 molecular weight polypeptide.

Amino acid analysis indicates that the alleles within the respective HLA-A and HLA-B genes are very similar to each other, but moreover, that the products of the HLA-A gene are very similar in composition to the products of the HLA-B gene. Biochemical similarity of the HLA-A, -B, and -C gene products and their common association with B₂-microglobulin clearly indicates that they have arisen by gene duplication. Furthermore, a common evolutionary origin with immunoglobulin is supported by a marked homology in amino acid sequence between B₂-microglobulin and the C₃H (third constant region of the heavy chain) domain of IgG. In addition, intrachain disulfide bridges define domains resembling immunoglobulin domains.¹¹

The HLA-D antigens are somewhat different, being composed of two noncovalent glycosylated polypeptides of molecular weights 33,000 and 28,000, with antigenic activity residing on the heavier chain. Data suggest that these two subunits may share larger regions of structural homology with each other, although no such relationship appears to exist between the two HLA-D polypeptides and those of the HLA-A and -B antigens.

CONCLUSION

The discovery of numerous associations between HLA and disease is on the edge of revolutionizing our perception of certain physiological mechanisms and pathological conditions. More than 100 human diseases have been studied in an attempt to establish whether or not the highly polymorphic HLA antigen system is involved in susceptibility (or resistance) to the condition. In addition to the dramatic association of HLA-B27 with ankylosing spondylitis, definite correlations have been found to exist in nearly half of the diseases investigated. But what do these population studies really mean?

Several explanations have been suggested and are the subject of current intensive research. First, however, it is necessary to distinguish clearly between "association" (such as occurs for most of the diseases studied) and "genetic linkage" (rarely found). Association is the non-random occurrence of two genetically separate traits in a population, whereas linkage is the occurrence of the two loci sufficiently close together on one chromosome. Moreover, one must bear in mind that different diseases may have different mechanisms, and furthermore, that some of these mechanisms blend into one another. 1) *Immune response genes*: it seems logical that gene functions regulating human immune response would be located in the MHC, as they are similarly mapped in the extensively detailed mouse and guinea pig MHC.^{28,29} The first disease associa-

tions observed were generally higher with the HLA-B locus antigens. With the subsequent description of B-cell-associated antigens and the HLA-D locus, closer correlations became apparent with these neighboring DRw antigens. The interrelationships between immune response (IR) genes closely linked to, and in linkage disequilibrium with, the gene products of the MHC (e.g. DRw antigens, T suppressor and helper cells) may now provide an explanation. Such an elaborate defense mechanism against pathogens could be provided by the selective pressures which have maintained such highly polymorphic antigen systems as exist in the MHC. 2) *Molecular mimicry* or cross-reactivity between a pathogen and a particular HLA antigen would cause a dominant susceptibility for individuals carrying the HLA antigen. Normal immune surveillance mechanisms fail to operate because the pathogen resembles a "self" antigen. 3) Cell surface components (e.g. HLA antigens) could serve as virus *receptors*. HLA antigens may also resemble the binding site of a cell surface receptor molecule for hormones or other physiological ligands, thus influencing endocrine function and/or cell interaction. 4) Effects of *complement (C') component* (also mapped within the MHC) deficiencies could also cause susceptibility to infections or give rise to autoimmune conditions.

These disease studies have provided true natural experiments which will allow clinicians and immunologists to analyze the spectrum of genetic and immunologic relationships of the major histocompatibility complex. The delicate mechanism of the normal human immune response may now be clearly detailed. In particular, we may better understand the means of defense against external aggression (e.g. cell and organ transplantation) and somatic mutation resulting in cancer. Moreover, the general applicability of HLA association as a means of identifying patients at high risk for certain diseases may expose their basic underlying pathogenetic mechanism. By typing for these histocompatibility antigens one may soon be able to confidently detect susceptible individuals, calculate accurately the risk run by a particular patient population (or even individual), and thereby initiate the proper preventative measures.

(After this general introduction to the basic science of human histocompatibility, future articles from this laboratory will deal with questions in specific areas of interest.)

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Radioisotopic Scans

How Well Do They Predict Metastatic Disease?

WILLIAM L. NEWKIRK, M.D.*

ABSTRACT

Thirty-three patients with known or suspected (and subsequently proven) malignant disease received radioisotopic scans within five weeks of their death and autopsy. A total of 51 scans were performed. Eleven of 13 (85%) of the brain scans were accurate. Twelve of 15 (80%) of the bone scans were accurate. Thirteen of 23 (57%) of the liver scans were accurate. These accuracy rates approximated the rates reported in well-designed studies from the medical literature. All 23 patients receiving liver scans had serum alkaline phosphatase determinations performed within one week of their scan. Twenty-three of 23 (100%) of the alkaline phosphatase determinations accurately reflected hepatic metastases.

INTRODUCTION

Physicians frequently use radioisotopic scans to determine the extent of metastatic disease in patients with malignant disease. They often rely on the scans' accuracy. Previous studies present conflicting views about relying on this accuracy. For example, in the case of liver scans, Rosenthal¹ examined 111 patients with extra-hepatic malignancy and concluded: "...the liver scan does not offer...[significant clinical information] in the detection of hepatic metastases." Hayes,² on the other hand, proposes routine use in lung cancer patients "with the expectation that these procedures will be helpful in selecting which patients need...therapy." Some of this confusion stems from the initial studies on the accuracy of radioisotopic scans. After reviewing five major studies on liver scans, Conn³ listed three criticisms:

1. Patients are not selected randomly. Patients with mild disease rarely come to surgery, biopsy, or autopsy. Studies which rely on these forms of confirmation will be skewed in favor of positive scans correlating with malignancy.
2. There were no defined time intervals between scanning and confirmation of disease. The assumption that a tumor found at autopsy represents the filling defect seen on scan months or years earlier, is disputable.
3. Studies utilize inadequate means of confirming the presence of malignant disease. Ozarda and Pickren⁴ found that 15% of all liver metastases cannot be detected by surgical exploration.

This study overcomes two of Conn's criticisms. First, it uses only autopsy findings to determine the presence of malignant disease. The study ignores

biopsies and surgical findings. Second, five weeks was the maximum time allowed between scan and autopsy. These two steps insure prompt and precise confirmation of scan findings. However, they also skew the study population toward patients with significant malignant disease. Accordingly, the findings in this study apply only to patients with known or suspected malignant disease and not to the general patient population.

METHODS

This study reviewed 674 autopsies performed over a two-year period at Miami Valley Hospital, Dayton, Ohio. Thirty-three patients from this group had proven malignant disease and had received a radioisotopic scan within five weeks of their death. The scans had been performed to determine the extent of metastatic disease. The origins of the patients' malignancies were:

Lung	12
Breast	5
GI Tract	5
Reproductive	3
GU Tract	2
Other	6

A total of 51 scans were performed:

Brain	13
Bone	15
Liver	23

The scans were performed on either a Phogama Camera[®] or a Picker Dynacamera[®] using these isotopes:

Brain	technetium 99 DTPA
Bone	technetium 99 pyrophosphate
Liver	technetium 99 sulfur colloid

All patients receiving liver scans had serum alkaline phosphatase determinations within seven days of their scan.

RESULTS

Brain Scans: Thirteen scans were performed. Three showed metastatic disease. Ten were normal. Autopsy revealed that two normal scan patients had brain metastases. The brain scan accuracy rate was 11/13 (85%).

Bone Scans: Fifteen bone scans were performed. Nine revealed metastatic disease. Six were normal. Autopsy confirmed eight of nine positive scans. Of the six patients with normal scans, two had bony metastases. The bone scan accuracy rate was 12/15 (80%).

Liver Scans: Twenty-three liver scans were performed. Nine showed metastatic disease. Fourteen

Continued on Page 371

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were normal. Autopsy confirmed eight of the nine positive scans. Nine of the fifteen patients with negative scans had liver metastases. The accuracy rate was 13/23 (57%). The serum alkaline phosphatase was accurate in all 23 patients. It was elevated in the seventeen cases with liver metastases and normal in the six cases without metastases.

DISCUSSION

Of the three types of radioisotopic scans, the liver scan is the least accurate in determining metastatic disease. Conn³ reviewed five studies of liver scans. Each study examined over one hundred patients. From these he found a 65% accuracy rate. In an excellent study conducted over a three-year period at Roswell Park, Gutierrez, *et al*⁵ correlated scan results with autopsy findings in cases of bronchogenic carcinoma. They used a ten-week time limit between scan and autopsy. Liver scan accuracy was 62%: 4% were false-positive; 34% false-negative. In this study, the liver scan accuracy was similar, 57%. The finding of 4% false-positive and 39% false-negative closely parallels Gutierrez's findings. The problem with using the liver scan to determine metastatic disease is that it is not a very sensitive test. Jhingren, *et al*⁶ note that 71% of 146 patients with proven liver metastases have an elevated alkaline phosphatase. This finding would indicate that alkaline phosphatase is more sensitive than the liver scan in determining liver metastases. The findings in this study indicate that serum alkaline phosphatase may be more sensitive than Jhingren's study would indicate. It proved to be accurate in 100% of 23 cases. In light of these findings, the clinician should be skeptical of liver scan findings which contradict alkaline phosphatase findings.

Gutierrez, *et al* noted an 87% accuracy rate for

brain scans. This study found a rate of 85%. They found an accuracy rate of 89% in bone scans. This study found 80%. Both brain and bone scans are reliable enough for clinical significance. However, the clinician should remember that they are still inaccurate between ten to twenty percent of the time.

CONCLUSION

This study evaluates the accuracy of radioisotopic scans in the determination of metastatic disease. The design of the study required prompt, precise confirmation of scan findings. Its finding of 85% brain scan accuracy and 80% bone scan accuracy are consistent with the medical literature. These two tests are valuable in determining metastatic spread of disease. However, only 57% of the liver scans were accurate. This finding was similar to numerous other studies and questions the value of the liver scan in predicting metastatic spread. The serum alkaline phosphatase is a more sensitive test of liver involvement. Physicians should view with special scrutiny liver scan findings which contradict alkaline phosphatase levels.

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Computed Tomography of the Spine

BARRY KUTZEN, M.D.*

INTRODUCTION

The spine is an inherently complex organ system and is difficult to completely image using conventional means. Recent advances in Hardware Resolution and Computer Technology have made C.T. an important and accurate means of displaying spinal anatomy and pathology, often supplanting more invasive procedures.

In this rapidly evolving technology, we have found C.T. most useful in the following circumstances.

1. Spinal Stenosis

Because C.T. demonstrates the spine in cross section, it is ideal for evaluation of spinal stenosis. The transaxial plane is optimal for obtaining cross sectional measurements (Figs. 1A,B).^{4,5}

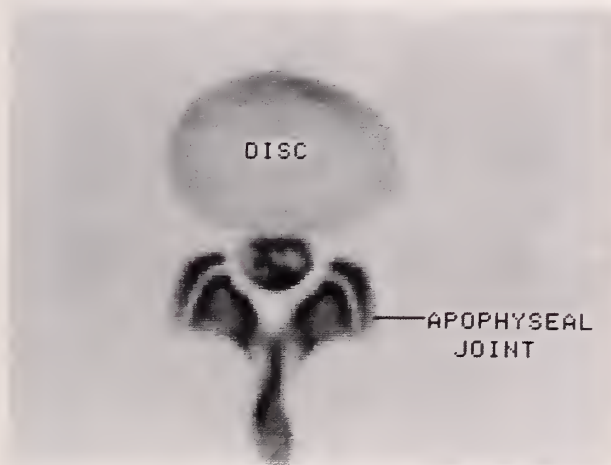


Fig. 1A

4. Disc Disease

The herniated and extruded disc can be demonstrated both with and without contrast material. C.T. can add additional information to the equivocal myelogram and at the same time the apophyseal joints and other spinal structures contributing to back pain can be elegantly demonstrated (Fig. 3).^{1,3}

5. Congenital Abnormalities

Spinal dysraphism can be more accurately demonstrated than with alternative means.

6. Neoplasm

Spinal, paraspinal and retroperitoneal disease and their extension into adjacent structures can be defined. C.T. is an optimal

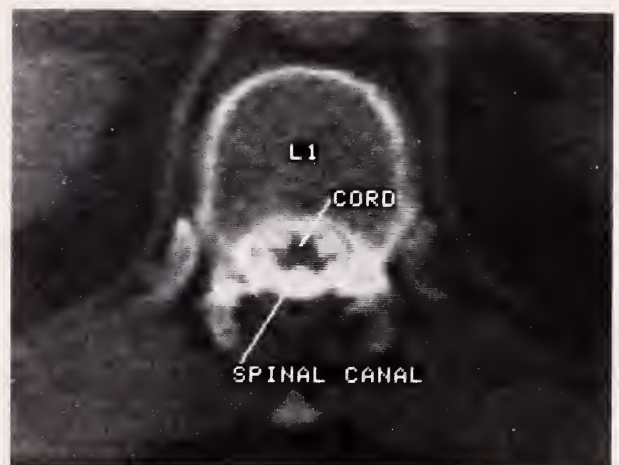


Fig. 1B

Fig. 1A. Normal anatomy of L4-5 disc with amipaque in spinal canal. Note how well apophyseal joints are demonstrated.

Fig. 1B. Normal anatomy at L1 demonstrates the relationship of spinal cord-canal-bony envelope complex. Aorta and diaphragmatic crura define adjacent retroperitoneum.

2. Trauma

The demonstration of the entire vertebral body and spinal canal complex on a single image is ideal for demonstrating the relationships of fracture fragments to the spinal canal as well as evaluating hematoma formation (Figs. 2A,B).

3. Postoperative

The sequelae of operative procedures such as hypertrophy of bone grafts, pseudoarthrosis formation and retained bone and disc fragments, often difficult to image by conventional means can all be displayed.

instrument for biopsy planning and localization (Figs. 4A,B).

PROCEDURE

Images were produced by a Pfizer FS 2000 scanner using fine collimation (4 or 8 mm.), a 256 or 512 matrix format and a special spine program. The scan time is generally 18 seconds. Because no localizer is present, a cross table lateral film is obtained to measure the lumbosacral angle for proper gantry orientation and the appropriate level is fluoroscopically marked on the skin as a starting point.

The examination is then tailored to the clinical symptoms at hand. The more specific the clinical information available the more specific and accurate the evaluation becomes.

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Fig. 2A



Fig. 2B

Fig. 2A. Automobile accident C.T. demonstrates degree of compression of spinal canal by fracture fragment. (L4)

Fig. 2B. Automobile accident note anterior hematoma displacing spinal cord posteriorly. (C4)



Fig. 3. Herniated disc fragment on the right at L4-5 compresses and displaces amipaque filled canal to the left, as well as amputates the nerve root sheath.



Fig. 4A

Fig. 4A. Carcinoma of the lung with unsuspected erosion into the spinal canal. This image also allowed for accurate biopsy.

Fig. 4B. Metastatic breast disease not only diffusely destroyed the vertebral body at L3 but markedly compressed the spinal canal.



Fig. 4B

CONCLUSION

We have found C.T. to be an effective modality in defining otherwise complex and difficult spinal anatomy. C.T. has the advantage of being non-invasive, presents anatomy in cross section without overlap and demonstrates surrounding organs. In combination with metrizimide enhancement, it becomes complementary in accurately defining intraspinal pathology.

The added dimension of the C.T. image has presented us with previously unobtainable anatomic relationships and detail.

It has been most useful in defining the suspicious myelogram allowing for higher confidence levels in surgical planning as well as post therapy evaluation.

Programs now in development will soon offer true three dimensional reconstructed images of the spine. The utilization of computed tomography is only limited by ones imagination.

Continued on Page 377

Rural Emergency Department Coverage

Comparison of a Physician Assistant to Rotating Medical Staff Members

WILLIAM NEWKIRK, M.D.*

ABSTRACT

Use of a physician assistant (PA) was compared to a rotating medical staff system as a method of providing emergency department coverage in a rural area. A 105 percent increase in utilization was seen on shifts covered by the PA, compared to a 19 percent increase seen on medical staff shifts during the same time period. This difference was statistically significant ($p < .01$). A financial analysis revealed that the PA generated a net revenue of 260 dollars per shift, while the medical staff system operated at a net deficit of 50 dollars per shift. Since the PA practiced without on-site supervision, methods to ensure quality of care had to be developed. Six methods were used. In the cases of 564 patients, the PA made no significant diagnostic or treatment errors. Each method of coverage has advantages for improving the quality of care.

INTRODUCTION

Rural emergency departments face certain problems not encountered by those in cities. One problem is adequately staffing the department with physicians when utilization is low. A traditional method is to have staff physicians take call on rotating basis. Frequently call is taken from home.

The emergence of the physician extender (physician assistant and emergency nurse practitioner) provides rural emergency departments with a new option for coverage. In 1974, Goldcomb and Herrold¹ studied utilization patterns in an emergency department and concluded that more than 50 percent of the care was providable by a physician assistant (PA). They wondered whether a PA would be able to cover a rural emergency department if he had adequate backup. In 1975, Maxfield, *et al*² described the successful utilization of a supervised physician assistant in a rural emergency department. Noble, *et al*³ (1975) described the use of emergency nurse practitioners (ENP) in a university emergency department setting. In 1977, Geolot, *et al*⁴ suggested that emergency nurse practitioners might be used to solve the "emergency care crisis in rural hospitals." Studies have shown a high patient acceptance of both PA's^{2,5} and ENP's.⁶ Physician extenders, within their limitations, have been shown to provide health care equal in quality to physicians in certain primary care settings.^{7,8} Despite this data, physician extenders have not been widely used in emergency care. In 1977, less

than 2 percent of physician assistants practiced in emergency settings.⁹

In 1979, Alongi⁶ cited the need for controlled studies of physician extenders in the emergency setting. A review of the literature for this paper revealed no controlled studies comparing the use of physician extenders to more traditional methods of emergency department coverage.

This study was undertaken to compare a coverage system utilizing a physician assistant to the traditional rotating medical staff system in a small rural hospital. The study focuses on the four main issues:

- 1) Would patients be willing to see a PA instead of a physician? Which practitioner would have the greatest impact on utilization?
- 2) What were the relative costs of the two systems?
- 3) How might adequate medical control be exercised for the PA?
- 4) What advantage would each system have for improving the quality of medical care?

METHODS

Redington-Fairview General Hospital is a ninety-two bed facility serving rural Somerset County, Maine. Prior to this study, the emergency department was staffed from 8 a.m. to 7 p.m. by a full-time emergency physician. Coverage from 7 p.m. to 8 a.m. was provided by a medical staff member selected from a call list. Beginning January 1, 1979, an ACLS-certified PA began covering the emergency department for approximately one-half the 7 p.m. to 8 a.m. shifts. The medical staff continued to cover the other half of the shifts. Utilization data was collected for both the PA and rotating medical staff shifts. Comparative data was collected from 1978. The study was continued for 140 consecutive nights, ending May 20, 1979. The charts of all patients seen by the PA were reviewed by an emergency physician within twenty four hours. Twenty-five cases were randomly selected for financial analysis. Statistical significance was determined by the Chi-square method.

RESULTS AND DISCUSSION

I. Utilization

Table 1 displays the utilization statistics. In the first group, 77 nights were analyzed. The staff physicians covered these nights in 1978. The physician assistant covered them in 1979. Utilization increased from 274 in 1978 to 564 in 1979. This represents an increase of 105 percent. In the second group, staff physicians covered 63 similar nights in 1978 and 1979. Utilization increased from 242 in 1978 to 290 in 1979. This represents an increase of 19 percent.

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In this study, the increase in utilization seen on shifts covered by the PA was large and statistically significant ($p < .01$) when compared to the increase in utilization seen on medical staff shifts. This apparent preference for the PA was surprising. Clearly, previous studies have shown excellent patient acceptance of physician extenders.^{2,5,6} Other factors may also be responsible. Stratmann and Ullman¹⁰ analyzed consumer attitudes toward emergency health care and highlighted the importance of the immediacy and accessibility of emergency care in patient utilization. Perhaps the major attraction to the PA was that he was always available in the emergency department; whereas the medical staff members were not.

TABLE 1

Coverage		No. of Patients Seen			
1978	1979	Number of Shifts	1978 No.(Avg.)	1979 No.(Avg.)	% Change
Staff Physician	Physician Assistant	77	274(3.6)	564(7.3)	+ 105%
Staff Physician	Staff Physician	63	242(3.8)	290(4.6)	+ 19%

II. Cost

Table 2 displays the relative costs of the two systems. Data was calculated per shift for comparison. For the medical staff system, hospital charges per shift were 160 dollars. Physician charges were 80 dollars. Lost practice time (valued at the local rate for emergency coverage) was 290 dollars. Thus the system lost 50 dollars per shift utilizing medical staff coverage.

When the physician assistant was covering, the net hospital revenue was 260 dollars per shift. There were no medical staff costs.

Based on these calculations, both the hospital and medical staff fared better with the PA than with the medical staff call system. Individual patient charges were the same.

TABLE 2

EMERGENCY DEPARTMENT COVERAGE COST COMPARISONS		
	Rotating Medical Staff	Physician Assistant
Hospital Charges per Shift	160	390
Hospital Costs per Shift	0	130
Hospital Net per Shift	160	260
Medical Staff Charges per Shift	80	0
Medical Staff Costs per Shift	290	0
Medical Staff Net per Shift	- 210	0
System Net per Shift	- 50	260

III. Medical Supervision

The third area of interest for this study was how to adequately supervise the physician assistant. Medical

supervision must review both the scope and performance of the PA's clinical practice. The scope of practice is limited by state law and medical staff privileges. In Maine, the state law is quite specific regarding what procedures the PA may perform and what drugs he may prescribe.

Supervising performance is more difficult because PA's generally practice without direct physician supervision. Using data from a national survey, Celentano¹¹ reports that greater than 70 percent of the PA's patient contact is without direct physician supervision. In this study, the PA practiced without direct supervision greater than 90 percent of the time. This required developing means to ensure adequate performance. Table 3 summarizes supervision options. Algorithms have been studied in both training¹² and primary care settings.¹³ Although diagnostic algorithms, both written and computer, were available to the PA, they were not necessary. Treatment algorithms were used for the treatment of cardiac arrhythmias. In most cases, the physician assistant used a list of treatment protocols selected by the emergency department staff. Under certain circumstances these protocols specified that the PA obtain specialty consultation.

Delayed supervision consisted of chart review, patient re-examination and retrospective audit. The charts of all 564 patients seen by the PA during the study period were reviewed by an emergency physician within 24 hours of the patient's visit. This provided the most important check of diagnostic accuracy. On occasion, if the diagnosis was questioned, the patient would be re-examined by both the PA and the emergency physician. In addition, charts were selected for retrospective audit. During the study, the PA made infrequent errors. These errors were in three categories: inadequate documentation; improper referrals; and minor deviations from treatment protocol. However, in the cases of 564 patients, the PA committed no diagnostic or treatment errors which had an adverse effect on the outcome of the patient's illness or injury.

TABLE 3

MEDICAL SUPERVISION	
Immediate	Delayed
1. Algorithms a. Written b. Microcomputer	1. Patient re-examination
2. Protocols	
3. Consultation	

IV. Possibility for Improving Health Care

The fourth area of concern for the study was what advantage each system had for improving the quality of care. Clearly there are advantages to using a physician. First, by law, the physician can have a greater scope of practice than does the PA: he has access to a larger formulary for treatment; he can perform a greater number of procedures. Second, the physician

has a broader educational base than does the PA, since the physician has had more indepth medical training. Third, in most cases the physician has had more experience seeing patients. Given the choice between an emergency physician and an emergency PA, one would select the emergency physician. However, comparing the PA system to the rotating medical staff system, one can see that the PA system possesses certain advantages. First, utilizing a PA requires the development of treatment protocols. The PA adheres to these protocols. Care is more consistent and of a predictable quality. Second, since there are fewer PA's than rotating medical staff members, it is easier to introduce new techniques and training to PA's than to all medical staff members. In this study, the PA completed instruction in Advanced Cardiac Life Support and MAST while the rotating staff physicians did not. The third advantage to the PA system is that emergency medicine is the PA's sole area of practice. The rotating physicians had to split their attention between emergency medicine and their own specialties.

CONCLUSIONS

In this study, the physician assistant coverage system proved superior to the more traditional rotating medical staff system in two areas. First, patients more readily utilized the PA than the rotating staff members. Second, both the hospital and the medical staff fared better financially with the PA system. Careful review of the physician assistants' performance indicated that care was provided in ac-

cordance with accepted protocol. Each system has certain advantages for improving the quality of care.

For small rural emergency departments a coverage system utilizing physician extenders may be preferable to the more traditional rotating medical staff system.

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COMPUTED TOMOGRAPHY OF THE SPINE—Continued from Page 374

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Total Knee Replacement in the Elderly

ROWLAND W. PRITCHARD, M.D.

INTRODUCTION

Total knee replacement has gained wide acceptance over the past five years as a definitive surgical treatment for severe disabling arthritis. In the elderly population, painful deformities of the knee joint can lead to severe loss of mobility and thus, social dependence upon others. The long-term results of total knee replacement surgery carried out by the author, in a small group of patients over 80 years of age, suggest that with few exceptions, these patients can be expected to do extremely well in terms of regaining mobility and function. The associated medical problems expected in this age group did not prove to be significant complicating factors—either in terms of the actual surgery or the hospital stay.

MATERIAL

Twenty-seven total knee replacement procedures have been carried out by the author in nineteen patients (the average age of 82.9 years) over the past five years. The oldest of these patients was a 90-year-old female in good physical health except for an unstable right knee, secondary to severe varus deformity associated with osteoarthritis. The youngest patient was an 80-year-old male suffering from carcinoma of the prostate and extreme left knee pain secondary to osteoarthritis. Of this group, there were 14 females, 6 of whom underwent bilateral total knee procedures. The remainder of the group was comprised of 5 male patients, two of whom underwent bilateral knee procedures. In all cases, the decision to undertake surgery was made because of unrelenting pain and disability relating to their knee deformities. Twenty-one of the surgical procedures were performed on knees with the diagnosis of deformities secondary to long-standing osteoarthritis. Five of the surgical procedures were carried out for the diagnosis of rheumatoid arthritis, while one surgical operation was performed for stabilization of a severely fractured distal femur in an 82-year-old female.

At the time of surgery, all patients were using external supports in order to ambulate. Two of the patients undergoing surgery had not walked for periods of over two years as the result of their knee problems.

TECHNIQUE

All patients were admitted to the hospital at least 48 hours prior to surgery for evaluation of associated medical conditions. Chest x-rays, cardiograms, blood and urine studies (including electrolytes, renal studies and urine cultures) were carried out routinely. Pulmonary function studies and blood gases were performed for baseline studies when indicated by history or clinical examination. In addition to their orthopedic examination on admission to the hospital,

all patients were thoroughly evaluated by an internist prior to surgery. Those patients with complicated medical histories were followed by the internist for the length of their hospital stay.

In all cases, spinal anesthesia was employed during the operation. The surgery, as previously outlined by the author,¹ required on an average one hour and 30 minutes from start to finish. All surgery was performed with the benefit of a pneumatic tourniquet and preoperative intravenous antibiotics were used in all cases. In no cases was postoperative anticoagulation employed since all of the patients were begun on ambulation by the third postoperative day. Hemovac drainage from the wound site was used for 48 to 72 hours and all patients received an average of 1.5 units of packed cells postoperatively as the result of direct blood loss from the surgery. Immediately following surgery, the involved extremity was immobilized in a canvas postoperative extension knee splint. This splint was removed on the third day after surgery, at which time the original dressing was changed. Thereafter, the splint was used only at night-time to maintain extension of the knee while the patient was sleeping. Postoperative intravenous antibiotics were administered for a period of 72 hours. In most cases, the antibiotic choice was Oxacillin; however, when a history of penicillin sensitivity was noted, this antibiotic was replaced with Keflin®. After discontinuation of the intravenous antibiotic, all patients were maintained on p.o. antibiotics until wound healing was secured and sutures had been removed. On the average, active flexion of the involved knee joint was instituted on the fifth postoperative day. If 90 degrees of active flexion of the involved knee joint was not achieved by the time of discharge from the hospital, manipulation of the knee was carried out under intravenous Pentothol® anesthesia. This procedure was necessary only in two individuals—each of whom had undergone bilateral knee replacements during the same hospitalization. With one exception, all cases employed the use of the Townley anatomic prosthesis. One case of severe fracture of the distal end of the femur in an 82-year-old female as the result of trauma, required insertion of a constrained Guepar hinge prosthesis.

HOSPITAL STAY

The hospital stay for a single knee procedure averaged 23.1 days in this age group. The shortest period of stay was 13 days and the longest period of stay was 76 days. This latter individual developed a mild stroke seven days after her surgery and required the extended hospitalization while recovering from her resultant hemiplegia. Of the two patients undergoing bilateral total knee replacements on one admission, the longest stay was 36 days and the

shortest stay, 28 days.

RESULTS

At the time of this study, 3 of the 19 original patients had died. The individual with carcinoma of the prostate died from metastatic disease approximately 9 months after his knee surgery had been undertaken. During the brief period of time between his surgery and his death, however, he was totally asymptomatic in terms of his knee pain and was able to ambulate independently. Two other females died from heart disease, one two years after surgery and the other four years after surgery. In each of these cases, the individuals had been active and free of pain up until the time of death. Of the 16 remaining patients alive at the time of this follow-up study, 5 patients were living in nursing homes and ambulating independently without pain. One patient was judged mentally incompetent and living at home with her family, but able to walk and complained of no knee symptoms. The remaining 10 patients were living at home alone or with their spouses and caring for themselves. Of this latter group, all patients stated that they were free of pain and only one was occasionally using a cane as an external support. Long-term range of motion of the operated knees varied from 85 degrees to 110 degrees of flexion. The longest follow-up at the time of this retrospective study was 52 months. The average follow-up was 26 months.

COMPLICATIONS

Review of hospital stay records suggest that postoperative confusion was the most frequent single complication in this group of patients. The onset of confusion developed, as a rule, 4 to 5 hours after surgery and usually could be traced to the use of either Valium® intra-operatively, or postoperative Demerol.® The confusion was generally more intense at night-time and often required restraint of the patient in order to prevent them from removing intravenous lines, Foley catheters, etc. In general, this type of confusion cleared within 3-4 days after surgery once pain medication could be tapered down.

Of the 19 patients operated upon, 10 were noted to have abnormal cardiograms upon admission. These cardiographic abnormalities varied from rhythm abnormalities to conduction defects and evidence of previous myocardial infarction. None of the patients operated upon showed any preoperative or postoperative evidence of congestive heart failure with one exception. This 82-year-old female developed atrial fibrillation several days after surgery. On the 8th postoperative day she suffered a stroke with resultant hemiplegia. She was hospitalized for a period of 76 days and eventually transferred to an extended care facility until recovery of her strength and balance had been achieved.

Other complications included an 84-year-old gentleman who developed a thrombosis of the femoral vein as a result of venous occlusion by the straps of a postoperative extension splint. This patient required surgical thrombectomy but went on to



Fig. 1. (Pictured in foreground), two years after bilateral total knee replacement surgery, this 87-year-old patient is shown with her family on a Shriners trip to Monaco. Now at the age of 89, she continues to function as a homemaker and cares for her husband. Prior to surgery she resided in a nursing home bound to a wheelchair.

have an excellent result from his knee surgery. Review of the charts failed to show any evidence documenting cases of postoperative pulmonary emboli, pneumonia, atelectasis or myocardial infarction. Of the 27 surgical cases carried out, there were no incidents of postoperative wound infections.

In respect to long-term follow-up, there has been no evidence of loosening of the component parts of the total knee replacements. One case of a fractured patella following insertion of a patellar prosthesis, was felt to be related to avascular necrosis of the remaining patella bone—probably as the result of surgical release of the lateral patellar retinacular ligaments at the time of surgery. This patients' fractured patella was treated with immobilization and went on to heal without significant loss of motion.

SUMMARY

In determining whether or not to carry out reconstructive orthopedic surgery on an elderly individual, the surgeon should base his decision on the physiologic condition of the entire body rather than on the chronologic age of the patient. Based on a review of this small number of cases, it would appear that elderly individuals over the age of 80 suffering from severe osteoarthritis of the knees who are in otherwise good general medical health can tolerate and benefit greatly from total knee joint replacement. Without this type of surgery, these individuals often become confined to wheelchairs and soon are prime candidates for nursing home care. It is the author's feeling that spinal anesthesia is an extremely important adjunct to carrying out this type of surgery in the elderly since it appears to place less stress on their cardio-pulmonary systems—and thus lower the rate of postoperative complications.

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MEDICINE SHOULD BE PRACTICED AS A FORM OF FRIENDSHIP"¹

RICHARD J. KAHN, M.D., F.A.C.P.*

Dr. Roland J. Wasgatt was born on March 9, 1873 in Ellsworth, Maine. He attended the common school, finishing his education at Bucksport Seminary in 1892. After attending Hahnemann Medical College he was appointed house surgeon of the Hahnemann Hospital in Philadelphia. In 1897 he began a private practice in Union, Maine.² A year later he moved to Rockland and practiced there until 1931, when he was killed in an automobile accident.

Well known and well loved, Dr. Wasgatt is fondly remembered by many of the older residents of the area. The following recollection was written by Ernest W. Maxcy, aged 73, of Camden, Maine. His boyhood memories serve to remind us that a physician should be a friend as well as a "purveyor of health care services."

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Roland J. Wasgatt, M.D.

A Tribute

ERNEST W. MAXCY

The time, February 17, 1913; the place, at home in Rockland amid the bustling of preparations for the wedding of one of my cousins in the town of Warren to which I had been invited. The plans were that I should accompany my parents, as you see I was only six years old. Everything in readiness, we boarded the trolley, on through Thomaston, then up the scenic trip along the river bank to Warren, then up the hills to my uncles farm where the festivities were to be held. Everything went as planned and all too soon we were on our way home again. On the way I complained that I felt ill, so as soon as we arrived at home I was trundled off to bed.

When I awoke in the morning it was apparent that I had a rather high temperature, so the doctor was called; the doctor, none other than Roland J. Wasgatt, the man who had brought me into the world, and who had saved my vision, when as an infant specialists had agreed that I would be blind. He arrived shortly before noon, first announced by his sleigh bells coming up the road. He burst in, and as was his usual practice, I believe that his overshoes landed in the front hall, his old buffalo coat in a heap on the living-room floor, hat and gloves could probably be found in the dining room, as by that time he was on his way to the kitchen to ascertain the source of the succulent aromas that were wafted through the house. After lifting the covers of a couple of pots on

the stove he proceeded to invite himself to dinner, at which he was always welcome. Now to look at the patient. When treating a child his first questions would be about school and if he received what he considered a brilliant answer, he would certainly take it home and try it on his own children and if the answer excelled that of his children, he would always report on his next call.

With his old cold stethoscope he was not long in determining that I had pneumonia. The treatment of this malady progressed satisfactorily but was complicated by the appearance of Empyema, or pus sacs around the lung, these the doctor attempted to treat, hoping at first to dry them up and later to tap them, much as you would a maple tree. Although I was getting the best of care, my general physical condition was deteriorating daily.

Somewhere along the line it was deemed necessary to engage a nurse. In those days registered nurses were scarce if not nonexistent, therefore a practical nurse was the usual alternative. In this case the nurse was Mrs. Cora Millay, a lady with three teen-aged daughters, whose husband had left his family and was cooking in a lumber camp. One of these daughters later became world famous, the well known poetess, Edna St. Vincent Millay. The doctor after exhausting every alternative decided that an operation was inevitable. In 1913 the only hospital in



Dr. Roland J. Wasgatt, 1909

the State that handled such cases was the Maine General in Portland. The only means of transportation was by rail and the good doctor feared, that due to my weakened condition that I could not stand the trip. This left but one alternative. He must do the job himself. The date was set for the operation. Here I recall, recounting a dream that I had on the eve of the operation. Awakening suddenly, I told my mother of dreaming of being in the Acorn Cemetery and telling her how cold and dark it was. What effect that must have had on her.

The next morning, a cold overcast day in the month of March the doctor arrived, accompanied by Dr. Alvin Foss, another of our general practitioners. The kitchen was selected as the operating room. The table had been previously scrubbed, so the team was ready, two G.P.'s and a practical nurse; no oxygen, no means of transfusions, nothing to back them up if things went wrong. They were supplied only by the contents of their usual black bags and a can of ether. The table was moved to the window for more light. An old sheet was torn up to supply gauze and bandages and was sterilized by baking in the oven, boiling water was available on the stove. The light from the window had to be supplemented by a gas light supported by a bracket over the end of the table. With a coal fire a few feet away, a gas light above and ether being administered between the two, why was there no explosion? A section of rib had to be removed and as bone grafting was unheard of in those days, there was no replacement. As I convalesced I recall two rubber tubes, draining the area, each with a safety pin through the end.

Today, 67 years later I can proudly display that scar as a mute testimony to the skill and dedication of those old time general practitioners. They whose monetary rewards were meager, but whose courage, skill and judgement was unexcelled.

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distributed and accepted.

No correspondence was reviewed.

Three applications to membership were reviewed. These included Drs. J. Bennett, D. Hegener and M. Nowtash. All three were unanimously voted into membership.

Dr. Grimes then gave an update on the Preliminary State Health Plan.

A report was given by Dr. Bach on the status of The Journal of the M.M.A. Discussion ensued as to the pros and cons of continuing the publication of this Journal. Following the discussion, a motion was made that the ACMA vote to discontinue the M.M.A. Journal. The motion was seconded and passed unanimously. Members endorsed the idea of a newsletter to replace the Journal.

Dr. Holler then reviewed the activities of the House of Delegates at the Annual Meeting of the M.M.A. recently held at The Balsams in Dixville Notch, N.H.

A preview of the fall meetings was presented to the members. This included the possibility of a joint meeting with Oxford and Franklin County Medical Associations.

Dr. L. Nadeau made a statement in regard to the loss of ACMA funds in reservations not kept. A report will be given at the September meeting as to the total loss of funds for the past year as a result of excess reservations. Also to be investigated will be the method of payment for cocktails during the social hour.

The meeting adjourned at 8:25 p.m.

EDWARD Z. WALWORTH, M.D., *Secretary*

York

The March meeting of the York County Medical Society was held on March 12, 1980 at Leedy's Restaurant in Alfred.

There was the usual social hour from 6:30 to 7:30 p.m. Following this, a most delicious dinner was served and the featured speaker of the evening was introduced by Dr. Conner Moore, President of our Society. The speaker was Ben Odom, C.P.A., Portland, Maine. His subject was "What the Physician Should Know About Office Management and Accounting." His talk was combined with a series of slides. It generated much discussion.

The business meeting was then called to order by our President.

The minutes of the last meeting were dispensed with in the interest of time.

Under old business was a presentation of the "Preliminary State Health Plan for Maine" by Dr. Carl Richards. He went into much detail concerning this plan and it was replete with much discussion following it.

The application of Dr. Roxanne C. Fiscella, of Saco, for membership in the York County Medical Society was presented. She was unanimously voted into membership by all those present. This was the only item under "New Business."

The following announcements were made by our President:

The May meeting of the York County Medical Society will be Wednesday, May 14, 1980 at the Cascades; however, it was left open to the committee if they wish to make a change.

The second announcement was the Interim Meeting of the House of Delegates to be held at the Mid-Maine Medical Center in Waterville on March 22nd.

There was no correspondence of importance nor was there any miscellaneous business.

The meeting was then adjourned.

There were 22 physicians and guests present.

MELVIN BACON, M.D., *Secretary*

Washington

A regular meeting of the Washington County Medical Society was held on May 27, 1980 at the Peavey Memorial Library, Eastport, with nine members present. Dr. James C. Bates, President, of Eastport, opened the meeting at 7:27 p.m.

I. Minutes of the last meeting, read and approved.

II. *Old Business:*

a) It was brought up at the last meeting, the question of dividing the County Society into two (2) sections, due to the size of the County, Eastern and Western, with the Eastern centered in

Calais and the Western in Machias. It was felt, however, that it would be better if we kept it as it is, but would try to hold meetings in a central area, that would be acceptable to most physicians, and with more physicians centered in the Machias area, most of the meetings will be held in that area.

b) Dr. Donald M. Robertson discussed the Washington County Physicians Quality Assurance Committee report, as well as the report of the Washington County Health Plan Program Review Committee. There was considerable dissatisfaction expressed, particularly because of the lack of physician input to this plan.

c) The following resolution was made; seconded and passed, "at a meeting of the Washington County Medical Society the proposed Quality Assurance Program and the proposed Washington County Health Care Plan, as prepared by the Washington County Health Plan, were discussed by the membership. Both plans are not acceptable in the present form by the County Medical Society. Your further comments and suggestions will be most welcome."

d) This letter will be sent to the President of the Washington County Health Plan.

III. The following resolution was also made, seconded and passed: "The Washington County Medical Society instructs its member on the Executive Committee of the Maine Medical Association, to oppose any further action on the Washington County Health Plan Quality Assurance Program by Pine Tree Professional Standards and Review Organizations, until this plan and the Associated Health Care Plan are modified to conform with the objectives and concerns of the Washington County physicians." Dr. Donald M. Robertson, member of the Executive Committee, was so instructed.

IV. Considerable discussion on Quality Assurance report, and the Washington County Health Plans, by Drs. Donald M. Robertson, Toby Aeheson, Richard Rowe and others.

V. Meeting adjourned at 9:30 p.m.

A special meeting of the Washington County Medical Society was held at the Congregational Vestry, Machias, Maine on July 1, 1980, with twelve members present. The meeting was held in conjunction with Washington County Health Plan to discuss mutual problems.

Dr. James C. Bates of Eastport, Maine, President of the Washington County Medical Society, was Chairman of the meeting. Approximately an equal number of the Board of the Washington County Health Plan was present at the meeting, including the President, Paul Plaut; Patrick O'Brien, Executive Secretary and Paul Weston, who acted as one of the principal spokesmen for the Washington County Health Plan.

Dr. Bates alternated between calling on a Medical Society representative and a member of the Board of Washington County Health Plan to state their views.

Dr. Donald M. Robertson of Harrington, Maine, M.M.A. Executive Committee member from Washington County, led the discussion of Quality Assurance. He outlined the procedure, which had been proposed by Dr. Peter Leadley, of the Pine Tree Organization. This Plan was developed in conjunction with the Maine Medical Association and an Ad Hoc Committee from the Washington County Health Plan and the Washington County Medical Society. The Plan has not been finalized as yet.

The main problem of the Medical Society members was they felt that they did not have sufficient input into the Health Care Plan that was presented to them, before they had time to peruse it and go over the various facets of the plan which would influence how they would practice, particularly, if they signed as members of the Washington County Health Plan.

The Medical Society would have liked to have gone over various parts of the Health Care Plan that they found difficulty with, along with the Board members of the WCHP, but due to limited time this was impossible.

It was therefore decided to appoint three members of the Medical Society: Drs. Donald M. Robertson, Eric M. Burke and Gordon Sears who will meet with an equal number from the WCHP and hopefully come up with a program that would be acceptable to both sides.

KARL V. LARSON, M.D., *Secretary*

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Dec. 11, 1980	Endocrinology Hugh Johnston, M.D., Maine Medical Center
Dec. 16, 1980	Diabetes in Pregnancy Paul Jones, M.D., Mid-Maine Medical Center—ITS Presentation
Dec. 18, 1980	Gynecologic Out-Patient Surgery John Makin, M.D., Rumford Community Hospital

The above activities are from 12-1 p.m. and have been certified
AMA and LCCME Category I. For further information contact
David Ginder, M.D.; 873-0621.

Mount Desert Island Hospital Bar Harbor, Maine

Dec. 12, 1980	Headaches H. Sandy Tamm, M.D., Eastern Maine Medical Center, Bangor
Dec. 19, 1980	Parkinson's Disease: Diagnosis and Management Merck, Sharp, and Dohme—Films

These conferences will be held in the SNF Conference Room,
Mount Desert Island Hospital; Fridays 11:30 a.m.—1:00 p.m.
These programs have been certified AMA/LCCME Category I.
For further information contact Christopher Brigham, M.D.;
288-5081.

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THE JOURNAL

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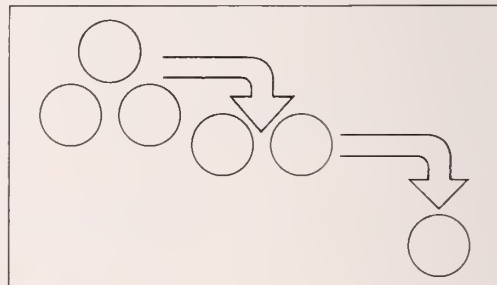
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Indications and Usage: For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. *Note:* The increasing frequency of resistant organisms limits the usefulness of all antibacterials, especially in these urinary tract infections.

Also for the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

The recommended quantitative disc susceptibility method (*Federal Register*, 37:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers; infants less than two months of age.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache,

peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for infants less than two months of age.

Urinary Tract Infections: Usual adult dosage—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

Recommended dosage for children—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. A guide follows:

Children two months of age or older

Weight		Dose—every 12 hours	
lbs	kgs	Teaspoonfuls	Tablets
20	9	1 teasp. (5 ml)	½ tablet
40	18	2 teasp. (10 ml)	1 tablet
60	27	3 teasp. (15 ml)	1½ tablets
80	36	4 teasp. (20 ml)	2 tablets or 1 DS tablet

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	½ the usual regimen
Below 15	Use not recommended

Pneumocystis carinii pneumonitis: Recommended dosage: 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

Supplied: Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10. Oral suspension, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole, fruit-licorice flavored—bottles of 16 oz (1 pint).



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